THE CONTRIBUTIONS OF DR. C. C. GUTHRIE

TO VASCULAR SURGERY

BY

Samuel P. Harbison, M.D., and Bernard Fisher, M.D.

BLOOD VESSEL SURGERY

AND ITS APPLICATIONS

BY

CHARLES CLAUDE GUTHRIE, M.D., Ph.D.

(A Reprint)

A Collective Review of Fifty Years of Vascular Surgery,
A Biographical Note on Dr. Guthrie,
and Dr. Guthrie's Complete Bibliography

UNIVERSITY·OF·PITTSBURGH PRESS

Library of Congress Catalog Card Number: 59-12564

Printed in the United States of America

INTRODUCTION

Over fifty years ago the following paragraph appeared in the *Interstate Medical Journal:*

"The transplantation of a segment of rabbit's aorta between the cut ends of a dog's common carotid artery may be taken as an illustration of the magnitude of the histological changes that may occur and yet the mechanical function of conveying blood remain adequate. Three weeks after the operation direct examination showed considerable enlargement and thickening of the segment. After eight months the largement both in diameter and length was much greater and also the thickness of the wall, yet the mechanical functioning was good. The gross arterial appearance of the segment was vastly changed, the walls being greatly hardened and transparent. The intima was perfectly smooth and glistening. On section the increased thickening of the wall was found to be in a large part due to an increase in the fibrous tissue. Here, then, we have excellent preservation of mechanical function, notwith*standing very great alteration in physical and histological structure.* Similar results are being observed in a dog into which a segment of cat's abdominal aorta was transplanted, more than ten months ago."[1]

This paragraph, based upon extensive, careful laboratory work, was written by Charles Claude Guthrie. The remarkable thing is that his findings were not exploited clinically (See Plate 6) despite the fact that Murphy, Halsted, Matas, and others knew of them. The experimental work had begun in 1905 when Alexis Carrel came to this country and was assigned to Dr. Guthrie at the Hull Physiological Laboratory of the University of Chicago. Dr. Carrel had published a simple, clear description of the technique of blood vessel anastomosis in 1902,[2] and wished to carry on further experiments in this field.

After several failures, using Dr. Carrel's method and carefully avoiding puncturing the intimal surface, Dr. Guthrie suggested they try including it in the stitches, and thereafter this technique was followed with uniform success. Later, Guthrie learned that this method was used by Dorfler in 1899 (*Blood-Vessel Surgery*, p. 2). Separation of the ends of the intimal surfaces as well as puckering was avoided, which reduced leakage and intravascular clotting, these later being further reduced by

[1]Some Practical Aspects of the Physiology of the Circulation. *Interstate Medical Journal*, Vol. XV, No. 6, February 29, 1908.

[2]*Lyon Medicale*, XCIII, 1902.

using smaller needles and thread, and later by applying oil or vaseline to the thread and tissues, especially with small vessels when longer exposure is required, which was established by his experiments at the University of Missouri.

Also, while at Missouri he conceived and developed the idea of transplantation en masse and by "patching," due to the difficulties they had experienced in kidney transplantations owing to the character of the renal vessels.

The two men worked together from the spring of 1905 until August of 1906. During this period they published jointly no less than 21 articles. (See Guthrie Bibliography) Their work included studies not only upon blood vessels themselves but upon the application of this technique of anastomosis to the transplantation of kidneys, limbs, and thyroids, as well as to reversals of circulation. (Later work of Dr. Guthrie included transplantation of a complete dog's head to the neck of another, with observations upon the state of consciousness of the

PLATE 1. *Photograph of transplantation of dog's head to neck of recipient dog. See Dr. Guthrie's text, pages 127 and 250.*

Chicago Monday.

Dear Dr. Guthrie

Many thanks for your letter, the threads and the outlines of your communication. I think it is very good. For the meeting of Ann Arbor, it would be interesting to say almost the same things. As it is a physiological meeting it is not necessary to insist very much on the technique. It would be better to speak about the results and the possible applications in physiology and a little in surgical physiology and surgery. Very probably I will go to this meeting. Can you do me the favor to write a paper about transplantation of veins and viscera, dealing principally with the results of the anastomoses and the possible applications to physiology? Do you think it is not the best? All the second part of your communication would have been interesting for physiologists, the first part being more interesting for surgeons. I do not wish to speak more than five or eight minutes, on account of my bad pronunciation. If I can I will bring some dogs to Ann Arbor.

I cannot write this paper, because I am busy to write one great article on Uniterminal and biterminal venous transplantation (in "Surgery, gynecology and obstetrics", about 10000 words and 20 figures. Besides I am tired, having had some stomach troubles, and I cannot write as quickly as I used. I would like extremely to talk with you about this article. We must publish it as soon as possible. We have blank card for the length of the article. And it will be published as soon as we will wish (This is due to Dr Bloodgood of John Hopkins who has written to the editor about this work).

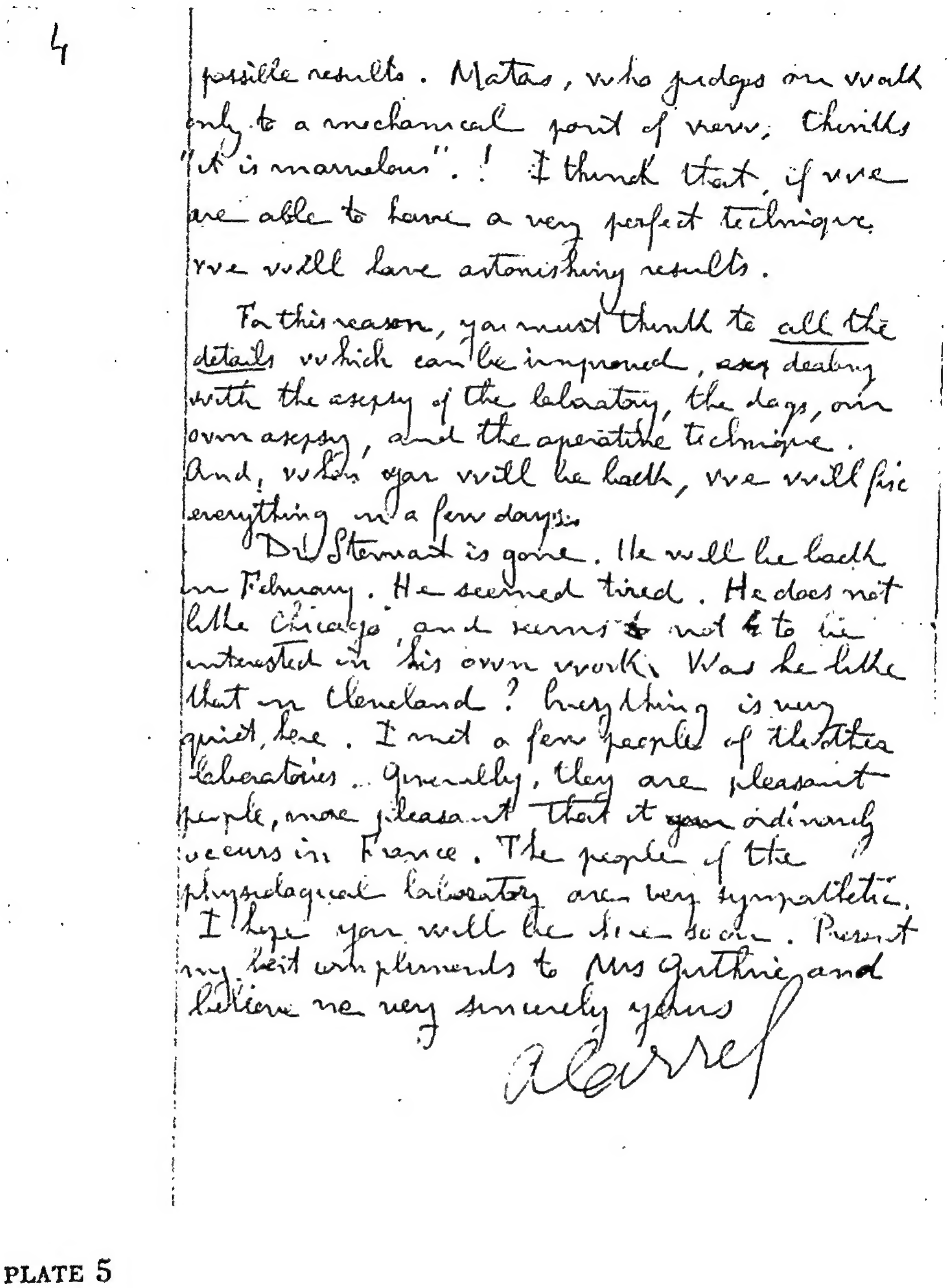
Your results [illegible] in anastomosing carotid and jugular are very good. I am very interested in your little scheme, showing

PLATE 2

donor head, thus pointing up the error of another Russian "first".) The description of these experiments will be found on pages 127 and 250 of Dr. Guthrie's text.

In August, 1906 Dr. Guthrie accepted the chair of Physiology and Pharmacology at Washington University in St. Louis and Dr. Carrel went to the Rockefeller Institute. However, the two men corresponded

very frequently after their separation, and all of Dr. Carrel's letters have been made available to the editors by Dr. Guthrie. One of these is reproduced in Plates 2-3-4-5. It is especially significant for its tribute to Dr. Guthrie in connection with his new suture material and its application. The references to Matas, Cushing and Bloodgood are interesting, as is also the statement "it is the beginning of a new plastic surgery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possible results. Matas, who judges our work only to a mechanical point of view, thinks "it is marvelous"! I think that, if we are able to have a very perfect technique, we will have astonishing results.

For this reason, you must think to all the details which can be improved, any dealing with the asepsy of the laboratory, the dogs, our own asepsy, and the operative technique. And, when you will be back, we will fix everything in a few days.

Dr Stewart is gone. He will be back in February. He seemed tired. He does not like Chicago and seems not to be interested in his own work. Was he like that in Cleveland? Everything is very quiet here. I met a few people of the other laboratories. Generally, they are pleasant people, more pleasant that it ~~generally~~ ordinarily occurs in France. The people of the physiological laboratory are very sympathetic. I hope you will be here soon. Present my best compliments to Mrs Guthrie and believe me very sincerely yours

A Carrel

PLATE 5

during the fall of 1905, continuing the experiments and performing new ones successfully in spite of makeshift facilities. Dr. Carrel expressed appreciation for suggestions of techniques and high praise for new suture material (the suture material referred to, was ravelings from a scrap of silk flour bolting cloth that Dr. Guthrie obtained from the miller in Columbia, Missouri). Also Carrel reported unsatisfactory results

from the experiments he was performing. In numerous other letters to Dr. Guthrie at Missouri, and for several years after their experimental work together ended, Dr. Carrel's letters consistently manifest his high evaluation of Dr. Guthrie's skill and ability in all phases of the work.

As previously stated, all this early work was a joint endeavor, shown by credit given to Dr. Guthrie in publications by Dr. Carrel, e.g., Alexis Carrel, *American Medicine*, August, 1905; Alexis Carrel, *LaPresse Medicale*, Samedi, 30 Decembre, 1905, No. 105, p. 843;[3] by their publications; by a special footnote in their paper from the Hull Laboratory, University of Chicago, in *Surgery, Gynecology and Obstetrics*, 1906, II, No. 3, March, p. 268;[4] and by letters from Dr. Carrel to Dr. Guthrie.

In his letters from the Rockefeller Institute, Dr. Carrel urged Dr. Guthrie to resume experimenting with him there, or he would come to St. Louis (November 23, 1907) . . . "sorry we cannot work together . . . I have planned . . . complicated operation . . . but I cannot accomplish it unless I should have as a collaborator a man like you, and I do not hope to find him . . . We should operate every day in the best possible conditions."

In 1912, Dr. Guthrie published his book *Blood-Vessel Surgery and Its Applications.* A letter from Dr. Guthrie's son describes the genesis of this book:

"He never wanted to write a book because he knew it would minimize or occupy all of his experimental research time.

"Even when Carrel (Oct. 19, 1905) suggested they write one together, he declined to consider it.

"While in St. Louis, C. V. Mosby repeatedly urged him to write a textbook on Physiology and continued doing this; after my father went to Pittsburgh Mosby personally came to see him and several times submitted very liberal contracts, all of which were promptly declined.

"He consented to write 'Blood Vessel Surgery and Its Applications' as one of the International Medical Monograph series at the request and urging of the Editor, Dr. Leonard Hill, only because he was convinced that it would be a valuable scientific contribution.

"The first manuscript submitted, covering only vascular anastomoses, transplantations, etc., was returned with very complimentary comments but also with the suggestion by the publisher that it be extended since

[3]"Pendant le seul mois d'Août, 1905, C. C. Guthrie et moi avons pratiqué 13 anastomoses arterio-veineuses, sans avoir un seul échec."

[4]"The work in this laboratory has been conjointly performed."

it was much shorter than previous volumes. They urged him to do so, if possible by including material from other, preferably related, fields in which he had worked—which no doubt explains the initial surpris that many experience on first scanning the last portion of it."

There are only a few copies left in Pittsburgh, where it was writte and it is little known elsewhere to judge by the bibliographies of rece writers. With this in mind, we have thought it important to preser the significant portions of the original work as an historical docume and tribute to the author. The table of contents and the index have not been altered. However, chapters VI, VII, IX, and portions of chapter VIII have been omitted.

Thus this volume contains Dr. Guthrie's contributions to blood vessel surgery; a biographical note and his complete bibliography; and a collective review of the development of vascular surgery from 1912 to the present. This review is the work of Dr. Fisher.

It is obvious from this book that the techniques necessary for vascular repair, suture, and organ transplantation were well worked out many years ago. It remained for advances in supportive care, anesthesia, and antibiotics to make the clinical application of these techniques practicable.

Samuel P. Harbison, M.D.

DR. J. B. MURPHY,
RELIANCE BUILDING,
100 STATE ST
CHICAGO

May 9th, 1908.

Dr. C. C. Guthrie,
Washington University,
St. Louis, Mo.

Dear Doctor:

I thank you very much for your recent reprints and congratulate you on the splendid original work you are accomplishing. You are certainly setting some high-water marks for your contemporaries and I rejoice in the success your labors are achieving.

Very truly :

PLATE 6

INTERNATIONAL MEDICAL MONOGRAPHS

General Editors { LEONARD HILL, M.B., F.R.S.
W. BULLOCH, M.D.

BLOOD-VESSEL SURGERY AND ITS APPLICATIONS

BY

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PROFESSOR OF PHYSIOLOGY AND PHARMACOLOGY, UNIVERSITY OF PITTSBURGH. FORMER PROFESSOR OF PHYSIOLOGY AND PHARMACOLOGY, WASHINGTON UNIVERSITY, INSTRUCTOR IN PHYSIOLOGY, UNIVERSITY OF CHICAGO; DEMONSTRATOR OF PHYSIOLOGY, WESTERN RESERVE UNIVERSITY, ETC.

ILLUSTRATED

LONDON
EDWARD ARNOLD
NEW YORK: LONGMANS, GREEN & CO.
1912

GENERAL EDITORS' PREFACE

THE Editors hope to issue in this series of International Medical Monographs contributions to the domain of the Medical Sciences on subjects of immediate interest, made by first-hand authorities who have been engaged in extending the confines of knowledge. Readers who seek to follow the rapid progress made in some new phase of investigation will find herein accurate information acquired from the consultation of the leading authorities of Europe and America, and illuminated by the researches and considered opinions of the authors.

Amidst the press and rush of modern research, and the multitude of papers published in many tongues, it is necessary to find men of proved merit and ripe experience, who will winnow the wheat from the chaff, and give us the present knowledge of their own subjects in a duly balanced, concise, and accurate form.

Among the great advances in medical science which have been made in the first decade of the twentieth century, one of the most amazing is set forth by Professor Guthrie in his admirable account of Blood-Vessel Surgery. Co-operating with Dr. Carrel, he became a pioneer in the successful development of the new technique, and by its means carried to a successful issue some most extraordinary experiments on the transplantation of vessels and organs, culminating in the grafting of both kidneys with segments

the dead and hardened graft. Such grafts act as a scaffolding for the ingrowth of fibrous tissue and the spread of the intima from the living vessel. Meanwhile the smooth inner lining of the dead graft adequately conducts the circulating blood.

The experiments of Carrel and Guthrie bring within the realms of possibility, under favourable conditions of locality, the removal of an aneurysm and the restoration of vascular continuity by the insertion of a sterilized graft taken from the post-mortem room.

The physiological application of the methods of blood-vessel surgery quickly followed on their perfection. Not only kidney, but thyroid autografts have proved adequate in function. It is possible for the surgeon to locate such organs in new places—*e.g.*, the kidney can be placed in the neck and functionate when supplied by the carotid artery. So far only the autografts of organs have continued to carry on their function for long periods of time. Heterografts succeed at first, but inevitably fail after the first few weeks. This is the disappointing but unanimous conclusion of the experimentors. Thus there is, at present, no temptation for the enthusiastic surgeon to try and graft one lobe of the thyroid or a kidney taken from a healthy donor. The poor man will not be tempted to exchange one of his sound kidneys for so much hard cash. It would be interesting to see whether a graft from one of a litter to another would succeed.

The limb of an animal has been removed and engrafted, and the limb has survived for many days; no one, however, has succeeded yet in obtaining a return of function in the limb. The cripple cannot yet hope to have grafted on him another leg taken from some unfortunate who had just been accidentally killed.

It is interesting to note that the experimental results obtained do not lend any support to the view that deficiency of an organ is necessary for the survival of a graft of that organ.

In carrying out autografts, Professor Guthrie has shown tha perfusion of the grafts with physiological salt solution is a di: advantage. Kidneys engrafted without perfusion give much bett results. He has found human hairs form excellent material fc stitching blood-vessels together. Such ligatures are easily obtaine and prepared.

His most astonishing results have been obtained by the successfı grafting of hens' ovaries (without vascular anastomosis). Th grafts have taken and lived, and the hens have laid eggs fron which chicks have been hatched. Pure black Leghorn hens hav been grafted with ovaries taken from pure white Leghorns, an *vice versa*, and the hens have been covered, some by cocks o their own hue and others by cocks of opposite colour. Spotted chickens have resulted, while all the controls have bred true The evidence is in favour, then, of foster-mother, or *soma* influence.

Professor Guthrie discusses the results in relation with "graft-hybrids" and Darwin's views of the same. Graft-hybrids are produced by joining two young stems or two pieces of potato tuber together, each piece being taken from a different variety. The plants thus raised yield numbers of new forms of tubers, many of which appear to be of intermediate character.

It is a question whether "soma influence" really was at work in Guthrie's experiments, or the alteration of nutritional conditions increased the number of variations arising spontaneously in the egg-cells. Those who are interested in the problems of heredity will find much of interest in these experiments.

In the last part of the book Professor Guthrie discusses Resuscitation and Shock, and gives an admirable account of the scientific evidence on which is established the period of survival of the organs after a temporary cessation of the circulation. The author rightly attributes traumatic or psychical shock to a general inhibitory

state, and is wise in his suggestions as to treatment of this condition.

Professor Guthrie has given us a most suggestive and valuable work, full of material of immediate practical interest to the surgeon, the physiologist, and to him who studies the problems of heredity.

LEONARD HILL.
WILLIAM BULLOCH.

December, 1911.

a vainglorious manner, is deplorable. The writer regrets his weakness in being conventional rather than sincere in this respect.

The work is intended to give the facts of blood-vessel surgery and its applications, but no doubt errors occur. As knowledge advances, statements that now seem warranted will cease to hold. But this, it would seem, is inevitable. In so far as seemed desirable, references have been given for the benefit of the reader desiring to investigate any part of the subject in the literature. The portion of the work devoted to discussion is of secondary importance or value, as it represents only the writer's views based on his knowledge and experience. It is "by theoretical considerations that our knowledge is (sometimes) advanced." So it is possible that this portion of the work may aid in the discovery of new facts, or further application of the facts, which is the sole excuse for its inclusion.

My thanks are due to a number of investigators who have kindly granted permission to use their materials freely, and a number of editors and publishers for similar permission in the use of copyrighted materials.

In conclusion, I desire to acknowledge my indebtedness to Professor Clyde Brooks, Dr. A. H. Ryan, Miss Frances Virginia Guthrie, and Mr. William Irving of my staff, for much aid in the preparation of the manuscript, in the correction of the proof-sheets, and so forth.

C. C. GUTHRIE.

Physiological Laboratory,
University of Pittsburgh,
December, 1911.

CONTENTS

The original Contents for Dr. Guthrie's book is reprinted exactly as it was, although certain portions of the text (Chapters VI, VII, parts of Chapter VIII and Chapter IX) have been deleted in this facsimile reprinting. (See Introduction by Dr. Samuel P. Harbison, page xii.)

PART I

CHAPTER I

HISTORY OF BLOOD-VESSEL SURGERY

CHAPTER II

SURGICAL TECHNIQUE

CHAPTER III

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CHAPTER IV

MORPHOLOGICAL RESULTS

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CHAPTER V

APPLICATIONS OF BLOOD-VESSEL SURGERY

CHAPTER VI *

ANÆMIA AND HYPERÆMIA AND THEIR EFFECTS ON TISSUES

CHAPTER VII *

THE EFFECT OF ALTERATION OF THE CIRCULATION ON GOITRE

Asterisks after Chapter heads indicate omissions in text.

CHAPTER VIII (193-222 and 252-299) *

TRANSPLANTATION OF TISSUES

CHAPTER IX *

RESUSCITATION

Asterisks after Chapter heads indicate omissions in text.

BLOOD-VESSEL SURGERY
AND ITS APPLICATION

PART I

CHAPTER I

HISTORY OF BLOOD-VESSEL SURGERY

Repair of Simple Vascular Injuries.

Until 1899 but a relatively small number of arteries had been repaired successfully by direct suture. It is recorded that in 1759 Hallowell closed a wound in a brachial artery by thrusting a pin through the margins of the wound and tying a thread about it. It is usually considered that this operation was successful, as the radial pulse remained quite strong. But a few years later Asman tested the method on dogs; none of his operations were successful. In 1881 Glück successfully repaired a wound in an artery by means of small ivory clamps. In 1889 Jassinowski proved that arteries could be successfully repaired by suture. He used fine curved needles and fine silk, and made interrupted (buttonhole) stitches placed close together. He endeavoured to avoid penetrating the intima. Out of twenty-six experiments, twenty-two were successful, and some of the specimens were not taken for more than three months after the operation. The next year Burci confirmed the results of Jassinowski. Only, in addition to using fine round needles and fine silk, he made continuous stitches. In 1897 Murphy reported successful results from having sutured vessels with fine silk. At the same time, and little later, Silberberg successfully sutured arteries, including the abdominal aorta. For the most part he employed a continuous suture of the finest silk, which was placed with Hagedorn intestinal needles. He did not lay much stress upon the point as to whether or not the intima should be included in the stitch. Previous to this time, most investigators emphasized the importance of confining the stitch to the outer vascular coats.

In 1899 Dörfler published the essential features of the method now so universally and successfully employed, the essential features being the employment of *fine round needles and fine silk, and continuous sutures embracing all of the coats of the vessel.* Of sixteen experiments, twelve were successful. He concluded that fine cambric needles and silk thread would give excellent results in suturing blood-vessels. And from the observation that the presence of an aseptic silk thread in the lumen of a vessel did not necessarily lead to changes which might interfere with the patency of the lumen, he concluded that the penetration of the intima was not contra-indicated. In fact, he recommended that all coats be included in the continuous suture. The method is also adapted to repairing veins.

Union of Vessels.

The first permanent union of two blood-vessels was accomplished in 1879 by Eck, a Russian surgeon. This renowned pioneer in the

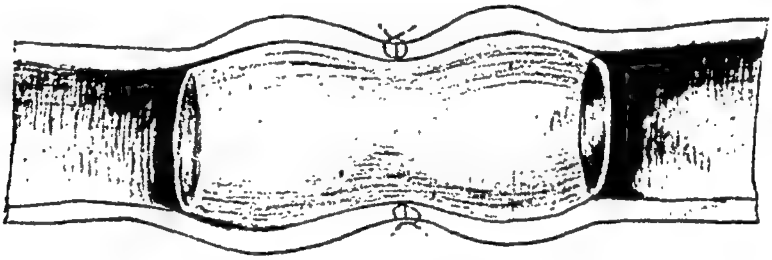


FIG. 1.—ABBE'S METHOD OF END-TO-END UNION OF BLOOD-VESSELS BY MEANS OF THIN GLASS TUBES.

field of vascular union successfully established a lateral communication between the portal vein and the vena cava. Thus, not only

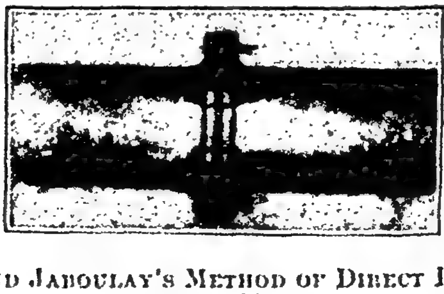


FIG. 2.—BRIAU AND JABOULAY'S METHOD OF DIRECT END-TO-END UNION OF BLOOD-VESSELS.

was the way opened for exploration, but the application of this operation by physiologists such as Minkowski, Pavlov, and others,

in the study of metabolism has yielded brilliant and far-reaching results.

V. Hirsch, in 1881, is accredited with having successfully sutured divided veins of dogs. In 1896 Briau and Jaboulay successfully united the ends of a divided carotid artery of a donkey by means

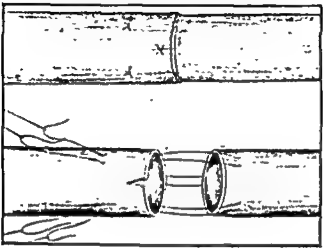


FIG. 3.—MURPHY'S EARLIER METHOD OF VASCULAR ANASTOMOSIS.

of U-shaped sutures so placed as to produce eversion of the edges of the walls and approximation of the intimas. Murphy, in 1897, published an invagination method carried out by means of silk ligatures, by which he successfully united the ends of divided arteries. Also he practised such anastomoses by means of con-

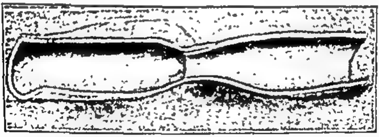


FIG. 4.—ENDS OF A BLOOD-VESSEL UNITED BY MURPHY'S INVAGINATION METHOD (*Medical Record*, 1897, 14), SHOWING THE USUAL CONTRACTION AT THE SEAT OF APPROXIMATION.

tinuous and interrupted sutures, one such operation out of five being successful. In 1900 Payr described a method of arterial anastomosis by invagination carried out by means of magnesium rings somewhat similar to the ivory clamps recommended by Nitze in 1897. Payr claimed to have used the method successfully. In

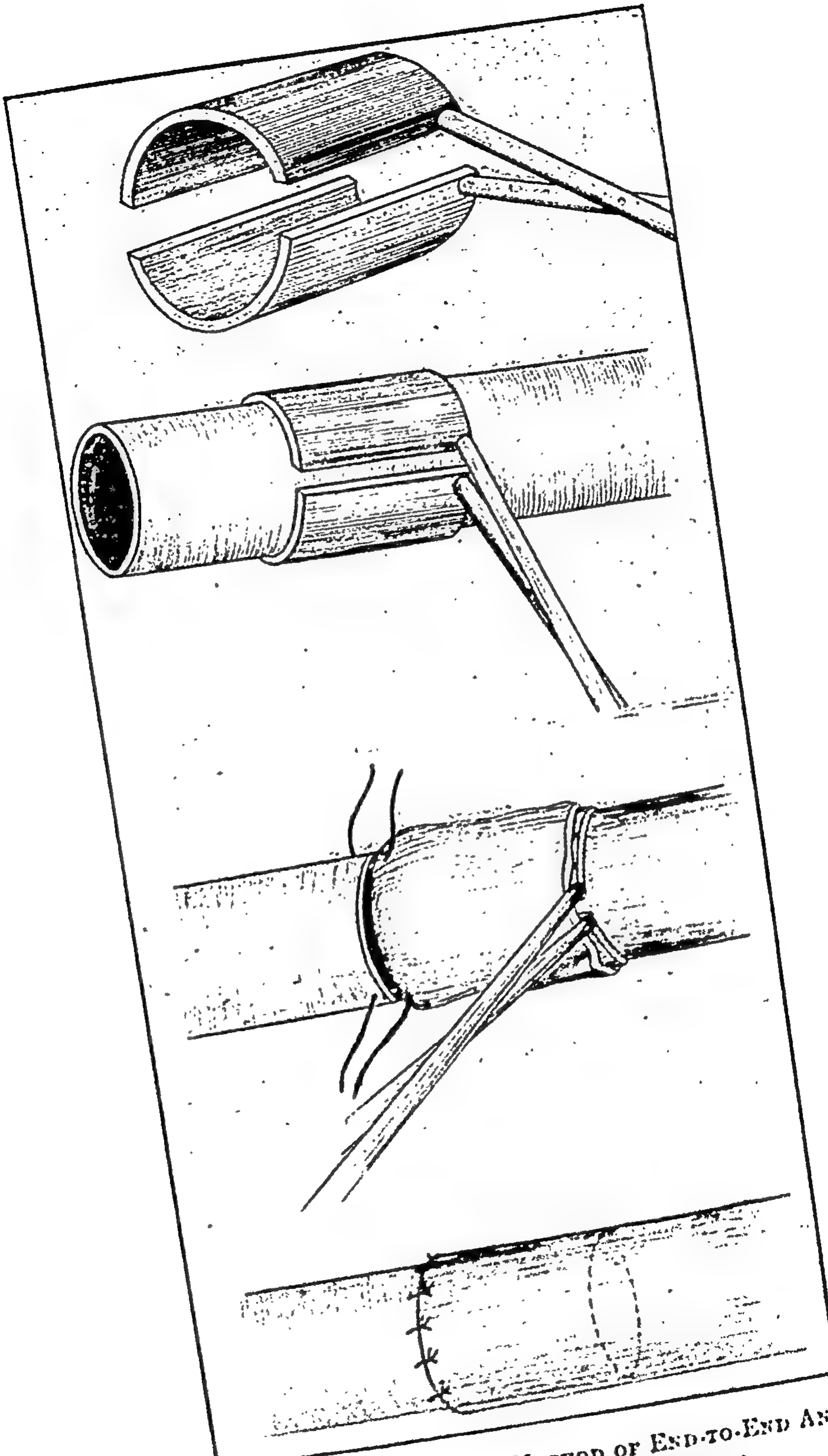


FIG. 5.—MURPHY'S MORE RECENT METHOD OF END-TO-END ANASTOMOSIS OF BLOOD-VESSELS BY INVAGINATION.

1901 Bouglé reported a successful arterial anastomosis by means of an invagination method, and also a successful result by simple end-to-end union by interrupted sutures. Fifteen days after the

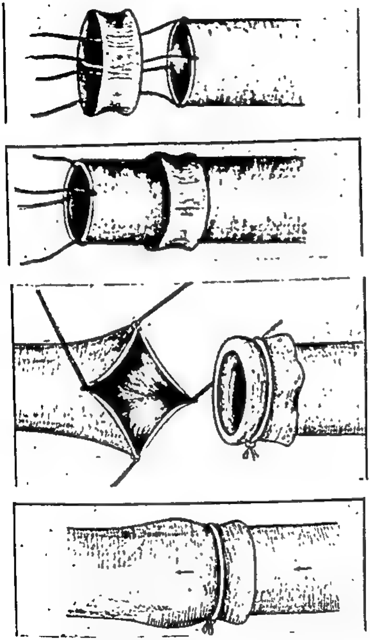


FIG. 6.—PAYR'S METHOD OF END-TO-END ANASTOMOSIS OF BLOOD-VESSELS BY MEANS OF ABSORBABLE RINGS.

operation both the vessels were patent and the intimas were smooth. In the same year Clermont reunited the ends of a divided inferior vena cava by means of a continuous fine silk suture, and a month later the lumen of the vessel at the point of operation was smooth

and unobstructed. In 1902 Tomaselli reported the results of eleven arterial anastomoses. He used interrupted sutures of fine silk. In seven of the cases successful results were obtained. In 1902 Salvia reported that out of sixteen anastomoses by Murphy's method two remained patent, though the lumen was narrowed. But six of these wounds showed infection. In the same year Berard and Carrel began the study of end-to-end arterio-venous anastomoses. The suture method they used was essentially like that of Dörfler, consisting in the placing of continuous sutures of fine silk by means of fine round needles. These investigators

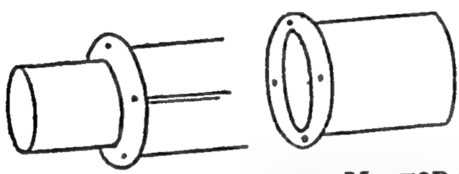


FIG. 7.—PAYR'S MODIFIED METHOD OF VASCULAR ANASTOMOSIS. (STICH.)

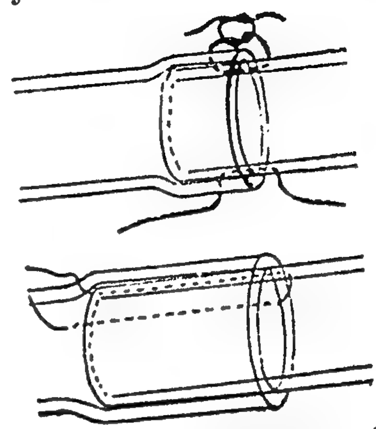


FIG. 8.—BOULGÉ'S METHOD OF VASCULAR ANASTOMOSIS.

differed from Dörfler in that they endeavoured to avoid penetrating the intima. The femoral artery and the saphenous vein of a large dog were exposed in Scarpa's triangle, and the central end of the artery was united to the peripheral end of the vein. The anastomosis adequately withstood the blood-pressure, but no physiological results were observed, as the animal died from infection two days after the operation.

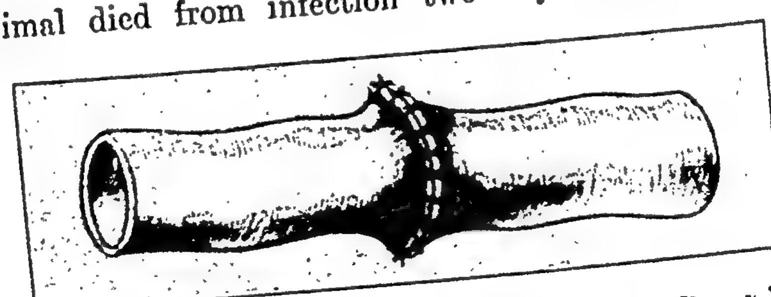


FIG. 9.—SALAMONI'S METHOD OF END-TO-END UNION OF BLOOD-VESSELS.

In another case the vessel was found to be occluded by a fibrous clot eight days after the operation. In an experiment by Carrel and Morel the peripheral end of a divided jugular vein was united to the central end of a divided carotid artery. This specimen was not examined directly, but several weeks after the operation the external jugular vein pulsated like an artery. In 1903

Jensen reunited the ends of divided veins by means of continuous sutures, which penetrated the intima, and of seven such operations four were successful. In the same year Höpfner reported the results of extensive studies on vascular anastomoses. He employed a circular suture of the vessels, and four of six arteries thus united were successful. He also reported having removed and success-

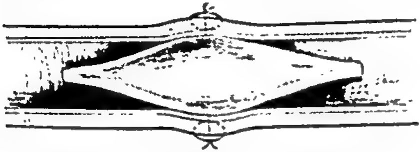


Fig. 10.—De Gaetano's Method of End-to-End Union of Blood-Vessels. (Keen's "Surgery," 1909, v. 133.)

ully replaced a segment of common carotid artery by means of ayr's magnesium ring method. One of the two operations of his description was proved to be successful by direct examination fter one month. In another experiment a segment of a dog's ommon carotid artery, more than an inch in length, was interposed between and anastomosed to the ends of one of the femoral rteries from which a similar egment had been removed, and the latter segment was interposed between the ends of the divided carotid artery. Examination two months later revealed smooth intimas and but little constriction, or, in other words, excellent results. He also successfully engrafted a segment of femoral artery of an animal between the ends of a carotid artery of another individual from which a segment had been removed. Floresco early in 1905 reported the results of numerous end-to-end anastomoses of arteries and veins which were performed in engrafting kidneys in dogs. The experiments were begun in 1902. So far as vascular anastomosis was concerned, he seems to have been successful.

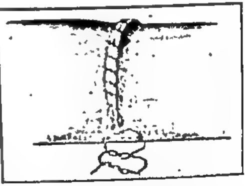


Fig. 11.—Dorrance's Method of Suturing Blood-Vessels.

In 1905 Carrel and the writer conjointly began experimenting with the anastomoses of blood-vessels in the Hull Physiological

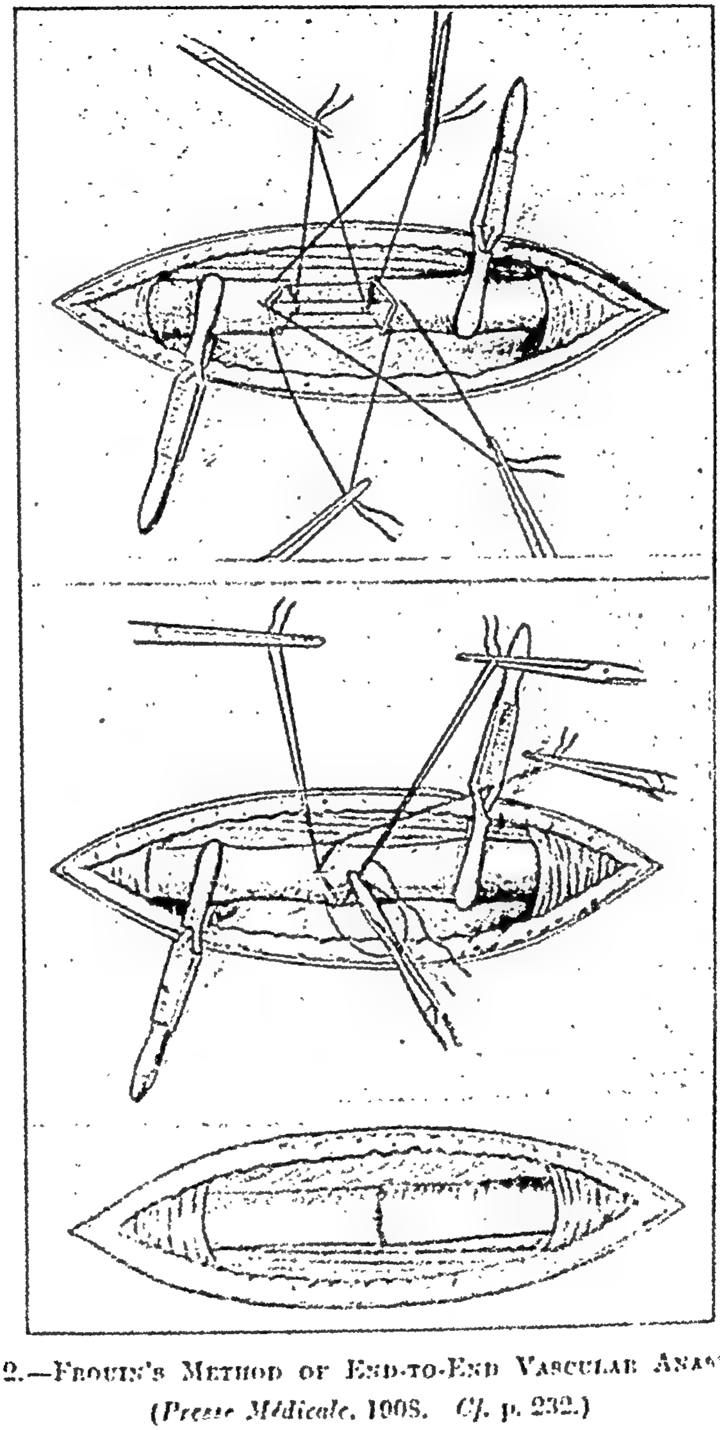


FIG. 12.—FROUIN'S METHOD OF END-TO-END VASCULAR ANASTOMOSIS. (*Presse Médicale*, 1908. *Cf.* p. 232.)

Laboratory of the University of Chicago, "with the view, among others, of making a complete study of the transplantations of veins. Several series of experiments were undertaken in order to study

the results of the uniterminal and biterminal venous transplantations, and they were thoroughly successful." The technique previously studied by Berard and Carrel and by Carrel and Morel in 1902 was first tried, but very soon the endeavour to avoid penetrating the intima was discontinued, and its inclusion in the stitches as recommended by Dörfler was practised. Other modifications were developed, until "finally we developed a technique which is equally well adapted for arterio-arterial, veno-venous, or arterio-venous anastomoses, and which yields uniformly successful results. This new technique has been used since 1905. Numerous arterio-venous anastomoses and transplantations of veins have been successfully performed." Especially noteworthy of these experiments is the constancy and perfection of the results of the vascular anastomoses, whether between arteries or between veins or between arteries and veins; the proof that the circulation through a vein may be reversed; the demonstration that a segment of vein may be successfully sutured to the ends of a divided artery to restore the continuity of the arterial lumen; that an opening in an artery may be successfully closed by a patch of peritoneum; and certain information regarding the engrafting of tissues with vascular anastomoses (which will be considered in the following division of this review). Watts, in 1906, repeated many of our experiments with confirmatory results

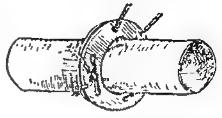


FIG. 13.—ANASTOMOSIS OF BLOOD-VESSELS BY MEANS OF METAL FLANGES. (LESPINASSE, FISHER, AND EISENSTAEDT.)

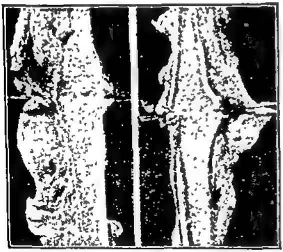


FIG. 14.—RESULTS OF ARTERIAL ANASTOMOSES BY MEANS OF METAL FLANGES. (LESPINASSE, FISHER, AND EISENSTAEDT.)

Common carotid operation. Dog killed 112 days later. The arteries were dissected out, and demonstrated to be pulsating. They were clamped and cut distal to the anastomosis. In each instance the blood spurted. The vessels were then split open and mounted. Age of operation, 112 days; magnesium practically gone; few small pieces still present; vessel smooth; no constriction.

(for figures, see Chapter IV.). In reviewing his results, he states "that of thirty-one experiments upon the vessels of the neck, twenty-eight were successful. . . . Also, that the results show conclusively that completely divided vessels can be sutured with a most uniform success, . . ." and that "the intima can be included in the suture with impunity, the application of the suture being thus greatly facilitated." Since that time the results have been reconfirmed by many other experimenters. In 1907 both Carrel and the writer reported successful results from repairing divided blood-vessels with segments of blood-vessels from different species of animals. Carrel transplanted segments of dogs' arteries which had been kept for some time in an ice-box into cats, two of five such operations being successful. The writer successfully engrafted a segment of the abdominal aorta of a cat and of a rabbit between the ends of divided common carotid arteries of dogs. In 1908 the writer successfully engrafted a segment of dog's vena cava which had been preserved for two months in 2·5 per cent. formalin solution, and then treated with dilute ammonia water, concentrated alcohol, and paraffin oil, between the ends of a divided common carotid artery of a dog. Carrel held that the tissue elements of segments of blood-vessels kept on ice for some time before being engrafted survived. But the writer, on the bases of the histological study of a segment of rabbit's aorta engrafted between the ends of a divided common carotid artery of a dog, and the successful engrafting of a formaldehyde-fixed segment of dog's vena cava between the ends of a divided common carotid artery of a dog, concluded that the elements of such engrafted segments to meet the vascular requirements need not, and probably do not, survive, but that for a time they may mechanically perform the circulatory function and serve as a bridge for the ingrowth of the other cells, and themselves ultimately suffer degenerative, disintegrative, and absorptive changes. For the segment of rabbit's aorta on dog's carotid was adequately transmitting the arterial blood eight months after the operation. Yet the gross appearance of the segment was vastly altered, being greatly enlarged, the walls thickened and hardened (calcified) (see p. 93 for detailed account). And, though performing an adequate circulatory function, the tissue elements of the formaldehyde fixed and absolute alcohol treated segment could not be considered to have survived.*

In 1910, with F. V. Guthrie, the writer announced that divided

* *Cf.* Carrel, *Jr. Exp. Med.*, 1911, xiv. 126.

blood-vessels could be successfully sutured together with human hair, the stitches being of the continuous variety and penetrating the intima. The chief value of this result, perhaps, is the knowledge that a suture material with which successful vascular operations may be performed is widely distributed. And, since it is not easy in all places to quickly obtain suitable thread for such suturing, it is by no means improbable that the fact that hair may be used may later be of practical value.

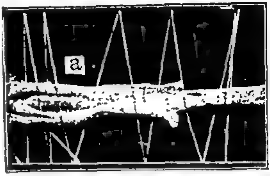


FIG. 15.—CENTRAL END OF LEFT COMMON CAROTID ARTERY ANASTOMOSED TO THE PERIPHERAL END OF THE LEFT INTERNAL JUGULAR VEIN WITH HUMAN HAIR.

Results of Vascular Suture in Man.

Up to the beginning of the last decade, though not absent, mention of successful vascular suture in man was rarely entered in the literature. And at least the majority of such cases reported belonged to the doubtful class, to be presently discussed, as regards conclusiveness of evidence of success.

Until 1900, according to Dörfler, but a very small number of arteries in man (nine) had been repaired successfully by direct suture. At this time two cases operated upon by Garré were added to the list. One of these consisted in the suture of one of the common carotid arteries on the removal of a tumour. The patient recovered, but died a few months later. No post-mortem examination was made. In the other case the brachial artery was sutured, and, though diminished, a pulsation of the radial and ulnar arteries persisted. The conclusion was drawn that both operations were successful. Other similar cases might be cited from the literature, but the two given are fairly representative, and will therefore serve, together with what follows, to illustrate the fallacy of drawing definite conclusions from such cases. But first it must be stated that it is assumed that in such instances the term "success" is employed to mean that the lumen of the vessel remained patent at the point of operation—at least, until primary healing of the vessel was complete.

In analyzing the observations presented in the report of the two cases, it is observed that in the case of the operation on the common carotid artery that no symptoms attributable to occlusion were

seen. Now it is known that in man ligation of one of these arteries is not necessarily followed by symptoms of circulatory deficiency. So it must be concluded that the observation reported proves nothing so far as preservation of patency of the arterial lumen is concerned.

The second case, which involved suture of the brachial artery, likewise proves nothing in this respect. It is true that the continuation of the radial and ulnar pulse strongly indicates at least a temporary preservation of the arterial lumen, for if such a vessel be ligated, pulsations in the distal trunks ordinarily for a time disappear or become impalpable. But, as Guthrie pointed out in 1830, as the extent of collateral circulation by way of anastomotic connections between different portions of the vascular trunks varies considerably, it is possible that in a case presenting unusually free connections of this character, ligation of the main arterial trunk would not diminish the circulation to the point of extinction of a detectable pulsation in the distal arteries. Also, it is known that the gradual occlusion of an arterial trunk is accompanied by the rapid development in size of anastomotic channels, so that at the moment the lumen of the vessel becomes completely closed, the collateral channels may be sufficiently large to transmit the pulse-wave. And for these reasons the observation of a pulse in the distal arteries is no proof of the success of the vascular suture. It may be remarked that Matas, by applying this principle, has evolved a method of causing ablation of aneurismal sacs.

Guthrie legitimately concluded from his numerous observations and the observations of others that gangrene, though not unknown, by no means necessarily follows ligation of the main brachial or femoral vascular trunks. So the absence of this dread complication after suture of such vessels with the view of permanent preservation of patency as direct circulatory channels is no proof of successful execution of the laudable intention.

As discussed more freely elsewhere (p. 69), even the abdominal aorta may be permanently occluded posterior to the renal vessels with at most but temporary clinical evidence of circulatory derangement in the posterior portion of the trunk and extremities. So the report of successful suture of such vessels cannot be accepted on evidence other than that furnished by direct inspection of the vessel at the point of operation. In 1902, according to Schmitz, twenty-one successful arterial sutures in man had been reported; and in 1903, according to Dörfler, the number had been raised to

thirty. In 1910 Stich stated that such successful operations numbered more than a hundred.

For some reason, until recently, fine gut and needles of the ordinary surgical type were employed for suturing blood-vessels. This, I believe, may be traced back to pre-anti- and pre-aseptic days, when the date upon which "the ligature came away" after a vessel was ligatured was almost invariably recorded. *During* this period large ligatures were employed—indeed, tapes were sometimes used. Guthrie was one of the first to recognize the advantage of a thin "well-waxed" ligature. But this type of ligature also "came away" by sloughing. So what must have been the condition of the wounds when tapes were employed—virtual setons!

But knowing of this state of affairs, and contrasting it with the clean healing of wounds, and the safety of deep-placed absorbable sutures after the dawn of modern surgical methods, it is perhaps not so surprising after all that even in comparatively recent writings is to be found the recommendation of gut as vascular suture material. Another curious angle of the subject is seen in the fact that for years prior to development of a successful suture method of vascular anastomosis almost the identical character of materials and method was employed for intestinal suture, the differences being not fundamental, but chiefly in size of threads and needles.

Results of Transplantation of Tissues by Vascular Suture.

In 1903 Höpfner, in v. Bergmann's clinic, reported the results of amputation and retransplantation of the hind-limb of a dog with reunion of the blood-vessels by Payr's magnesium ring method. Good results were obtained for eleven days, at which time the animal was killed with chloroform. In 1905 Carrel and the writer repeated this experiment, using the suture method for anastomosis of the blood-vessels. Other similar experiments have since been performed, but the results achieved have advanced our knowledge but little beyond the stage attained from the experiments reported by Höpfner—that is to say, no one has as yet observed the return of function in the replanted or transplanted limb.

Ullmann, in 1902, removed and transplanted a dog's kidney into the cervical region, uniting the renal and carotid artery and the renal and external jugular vein by Payr's method. The kidney secreted for a time after the operation. In the same year v. Decastello performed similar experiments. In a case where he engrafted a dog's

kidney into another dog over a litre of urine was secreted by the engrafted organ. But, owing to a hæmorrhage, the animal lived a little less than two days. Floresco, in 1905, reported the results of numerous renal engrafting experiments which he began in 1902. He recommended circular suture of the blood-vessels, and that the organ be engrafted into the abdominal cavity. One of his animals lived for more than a month after one of its kidneys was removed and replaced by a kidney from another dog (see p. 230). But he did not present proof of permanent functional survival of an engrafted kidney. He collected and analyzed urine from engrafted kidneys; also he studied the structure of such kidneys. He tested various methods of preventing coagulation in the vessels of kidneys during the engrafting operation, as the injection of salt solutions to displace the blood, and the injection of peptone solutions and solutions of leech extract into the general circulation prior to the operation, in order to decrease the coagulability of the blood. He seemed to consider that the injection of salt solution into the kidneys was not, perhaps, a harmless procedure.

Carrel and the writer, in 1905, performing similar renal transplantations, obtained similar results. After devising a new method, which we termed "transplantation in mass," by means of which it was possible to transplant both kidneys by removing and engrafting segments of the aorta and vena cava bearing the renal vessels, they succeeded in keeping animals alive with wholly engrafted renal tissue for a longer time than had been previously reported. Dogs and cats were used in the experiments. Some animals lived for weeks after their own kidneys had been removed and replaced by kidneys from other animals of the same species. Since that time Carrel and several other experimenters have succeeded in keeping an animal alive even for months with its own renal tissue after it had been removed and re-implanted. Owing to the unsatisfactory nature of the results obtained with Carrel, especially as regards lack of permanency, the writer early came to the conclusion that the perfusion of the kidneys with salt solution, which was practised in the experiments, in itself was not above suspicion of being a harmful agent. Therefore, a series of experiments to test this point were carried out by him, and the results proved that salt solution had such an action (1907-08). A large number of cats were experimented upon by temporarily clamping off a segment of the aorta bearing the mouths of the renal arteries, and displacing the blood from the kidneys with salt solutions introduced into the aortic

duction of an internal secretion, but fertile eggs have been obtained from such ovaries, the proof of fertility being that healthy chicks have been hatched from the eggs. These results are more fully dealt with later (p. 270).

The view has been advanced that a necessary condition for the survival of an engrafted tissue is deficiency of such tissue in the animal into which the graft is made. But the writer's results speak emphatically against this view, though it must be added that as yet proof of possible permanent multiplication of tissues or organs in an animal is lacking. And certainly the view that has been expressed that to successfully engraft the tissue for even a short period it is necessary to create a deficiency in this tissue is erroneous.

REFERENCES.

The titles of the periodicals frequently referred to are abbreviated as follows:

Am. J. of Phy. = American Journal of Physiology.
Ar. of I. M. = Archives of Internal Medicine.
B. M. J. = British Medical Journal.
C. R. de la S. de B. = Comptes Rendus de la Société de Biologie.
D. Z. f. Chir. = Deutsche Zeitschrift für Chirurgie.
Jr. of Exp. Med. = *Journal of Experimental Medicine.*
Jr. of the Am. Med. Assoc. = Journal of the American Medical Association.
J. H. H. Bul. = Johns Hopkins Hospital Bulletin.
Jr. of Phy. = Journal of Physiology.
S. G. and O. = Surgery, Gynecology and Obstetrics.
Wash. Univ. Bul. = Washington University Bulletin.

ABBÉ: N. Y. Med. Journ., 1894, Jan. 13.
ASMAN: Dissertatio inauguratio, Groningue, 1773.
BORST AND ENDERLIN: D. Z. f. Chir., 1909, xcix. 54.
BOUGLÉ: Ar. de Méd. Exp. et d'Anat. path., 1901, 205.
BRIAU AND JABOULAY: *Lyon Méd.*, 1896, 97.
BURCI: Atti della Soc. Toscanadi di Sc. Nat., 1890, xi.
CAPELLE: Berl. Klin. Woch., 1908, xlv.
CARREL: Lyon Méd., 1902; Proc. of the Soc. for Exp. Biol. and Med., 1910, vii. 80; J. of Exp. Med., 1907, ix. 226; C. R. de la S. de B., 1909, lxvi. 419.
CARREL AND GUTHRIE: Science, N.S., 1905, xxii. 473, 565; C. R. de la S. de B., 1905, lvii. 518, 596; *ibid.*, 1906, lviii. 529, 582, 596, 730; Science, N.S., 1906, xxiii. 584, 589; Am. Jr. of Med. Sc., 1906, 297; Sept., 1906; Annals of Surgery, 1906, xliii. 203; S. G. and O., 1906, ii. 266.
CARREL AND MOREL: Lyon Méd., 1902, xcix. 114.
CLERMONT: Presse Médicale, 1901.
DE GAETANO: Giorn. Interna. delle Scienz. Med., *1903, 25.*
DORFLER: Beiträge zur Klin. Chir., 1899, xxv. 781; *ibid.*, 1900, xxv., No. 3.
DORRANCE: Annals of Surg., 1906, xliv. 409.
ECK: Trav. Soc. d. Natur. de St. Pétersbourg, 1879, x.

common under less perfect conditions, which would have left the question in an uncertain state for a much longer time. For the failures would have been due to infection of the wounds, etc., and yet it would not have been clear to the investigator that such was the cause; so the experiments would have been unnecessarily multiplied and prolonged, and time needlessly wasted before perfectly definite conclusions could have been drawn.

Since it is believed that the surgeon contemplating the suture of blood-vessels in man will, if conditions permit, beforehand familiarize himself with the operation on a lower animal, a sufficiently complete account will be given to enable him to duplicate our experiments to any degree that he may desire. Therefore, if I err in the matter of details, I pray that it may be rather on the side of too many than too few.

Animal Quarters.

In experimental work on animals, receiving facilities and quarters for keeping them in good condition are necessary. In the case of dogs such quarters should consist of at least two dry, well-lighted and ventilated rooms. The location of the rooms in relation to other buildings is an important consideration. For dogs, even under ideal conditions, are apt to be noisy, and are therefore apt to be a nuisance. In large buildings the most practical location is near or on the roof, if the roof be flat, in which case it is usually possible to utilize the roof for outdoor exercise space.

The rooms should have cement or other form of waterproof walls and floors, and the floors should slope to drains to facilitate cleaning. A tap and sink should be conveniently located, and a hose and connections provided for the tap, so that the rooms may be flushed out thoroughly from time to time. A room 10 feet square will accommodate from five to ten dogs, depending upon their size. If vagrant dogs are received, they should immediately have a numbered metal tag affixed to their neck by means of a collar. For this purpose insulated copper wire is very good, taking care to wrap the ends well to avoid scratching the skin. The number should be recorded, together with the date and a description of the animal. The animal is then placed in the room with the animals most nearly of its size. It should be watched for a time to prevent its fighting or preventing any of its companions from pitching upon it. An intelligent and well-trained animal attendant will be able to quickly discover any peculiarities of an animal, and to quarter

.s to preserve the greatest harmony in the kennels. The dog ımpanionable animal, and, except in rare cases, it is better to ı number of them together. As a rule, if there are ten dogs ıer, and fighting is heard, one animal is at the bottom of it, competent attendant will quickly locate and remove it, after the others will soon subside. But occasionally a "killer" ɔe received, and such animals are sometimes hard to detect. ıroper attention and tact on the part of the attendant will t insure harmonious relations between the animals.

: quarters should be kept scrupulously clean and orderly, requires daily sweeping and bedding. Sawdust is good for ng, owing to its absorbent qualities. Judgment should be n scrubbing, but it is not usually necessary to daily scrub the floor. While the room is being cleaned and ordered, it is ;o turn the animals into the outdoor exercise space. It is o allow the animals access to this space all the time; but if tions do not permit this, they should be turned out as long ssible each day. Each room should be supplied with fresh : all the time. Vessels for this purpose should be of such cter that they may be easily cleaned. Broad-bottomed pans very well. An abundance of good mixed food should be ied daily at a regular time. Here, again, the attendant must ise judgment in order to prevent fighting, and to see that animal receives its share. It is well to feed outdoors if pos- The food should be placed in pans or trays, and after the als are satisfied, all scraps, excepting a few bones, should be ved, and the vessels washed. Any bones left the next day .d be removed before feeding-time. The food may be obtained many sources, but I have found high-class hotel or restaurant ɪs the most satisfactory. The animal attendant leaves one or clean buckets fitted with lids each day at the time he goes ıe feed, and the servants throw meat, bread, gravy, and potato ɔs into them, so they are ready by the next day. On this diet ınimals thrive better than on ordinary butcher's scraps, and also much cheaper.

ıimals kept in confinement are especially prone to contract ge and other insect troubles, and it is necessary to exercise h care to keep them free of such pests. Mangy dogs, if received, ld be isolated and washed with a mild soap and warm water, thoroughly rubbed with sulphur ointment. A good ointment be prepared by mixing flowers of sulphur and lard together.

enamelled hand-basins, leg-tapes consisting of torn muslin strips 1 inch wide and 2 feet long, purified (surgical) ether, and large coarse towels, are essential. The potassium sulphite method of removing the hair has not been employed, but it is successfully employed in similar animal experimentation.

The sterilizing-room contains a sink with hot and cold water, toilet and surgical soap, brushes and a brush disinfecting pan, an instrument sterilizer of common form, a dressing sterilizer of the autoclave type or one using superheated steam, stands or tables and burners for the sterilizers, burners and tripods for boiling water, salt and other solutions, and one or more enamelled-topped or glass-covered deal tables for the preparation of instruments and dressings for the sterilizers, and a cupboard for gowns, dressings, etc.

The operating-room is equipped with an adjustable operating-table and accessories, a rack for basins, instruments, an instrument-table, a dressing-table, a heating apparatus such as a gas-stove to insure the maintenance of any desired temperature, a perfusion apparatus, compressed air or a small bellows for artificial respiration, and a movable light with reflector.

Preparation of Instruments and Materials.

The needle sused for suturing blood-vessels are of the ordinary polished steel cambric variety, ranging in size from the large No. 12, to the smallest, No. 16. The shaft of the needle tapers slightly to both extremities. The eye is small and oval in shape. Such needles are susceptible to rust, and for this reason it is not advisable to use them more than once. Needles with enlarged eye-ends are not suitable. The kind of suture material used for blood-vessel suture is very important. Fine silk is probably best for general work. There is a very great difference in silk, and only a first quality, long, smooth-fibred variety should be selected. Ravellings from silk bolting cloth, such as is used by millers for screening flour, are excellent. A similar thread is sold under the trade name of "bead silk."*

Such threads consist of three strands twisted together, and each strand is composed of two smaller strands. So the thread is made up of six small strands, and it can readily be split into three double

* Suitable needles may be procured of Kirby, Beard and Co., Ravenhurst Works, Bradford Street, Birmingham; and suitable silk of James Pearsall and Co., 71, Little Britain, London, E.C.

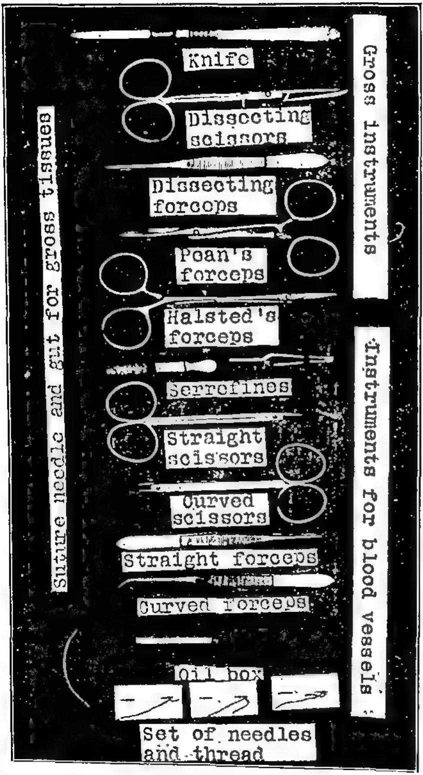


FIG. 18.—AUTHOR'S SET OF INSTRUMENTS FOR OPERATIONS UPON BLOOD VESSELS.

Only one of each type of forceps and clamps is shown.

or six single strands. The unsplit thread may be successfully employed on the larger arteries, such as the common carotid, but for smaller vessels it is better to use the single strands, either doubled or single, depending on the size of the vessel.

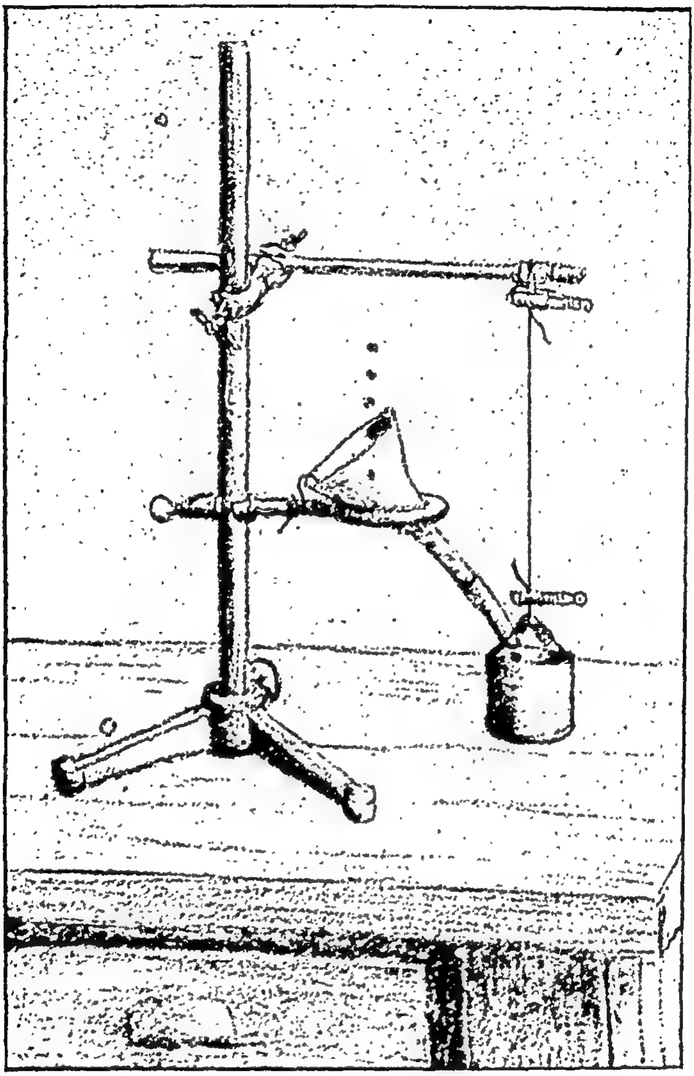


Fig. 19.—Apparatus used for Testing Suture Material.

Shot are passed into the cup by means of a funnel until the thread breaks, w always takes place at a point between the clamps. The cup and cont are then weighed. The blades of the clamps and other points that com contact with the thread are shielded with rubber.

Test for size may be roughly made by tossing the strand into still air of a room, and noting the time required to fall througl given distance. Smoothness may be tested by taking a small sti in the outer layer of the skin of the palm of the hand and draw the thread through. A rough thread should not be used.

Tests for strength may be carried out by the simple method shown in the figure. The following table shows the results of some tests of this character:

SUMMARY OF TESTS OF SUTURE MATERIALS.

	Strand.	Normal.	Sterilized in Oil.	Formalin (10 per cent.).	Remarks.
		ozs.	ozs.	ozs.	
SILK	1	2·63	3·08	1·91	Average of individual strands or hairs based on three or more tests. Greatest variation in test on individual strand, from maximum to minimum, about 16 per cent.
"	2	3·00	3·50	3·50	
"	3	—	2·83	—	
"	4	—	1·91	—	
"	5	—	3·58	—	
"	6	—	2·41	—	
"	7	3·82	—	—	
"	8	3·82	—	—	
"	9	2·75	—	—	
"	10	2·10	—	—	
Average ..		3·03	2·88	2·70	
HAIR:					Length, 55 centimetres. Variation in breaking-point of individual hairs less than in silk. Four tests to each.
Blonde L. G.	1	4·56	4·50	3·18	
" "	2	4·00	4·18	3·50	
" "	3	4·37	3·50	4·37	
Average ..		4·30	4·05	3·68	
Brown E. ..	1	3·93	4·62	4·00	Length, 65 centimetres. Eight tests on normal, four on others.
" ..	2	—	3·37	3·06	
" ..	3	—	3·56	3·68	
Average ..		3·93	3·85	3·58	
Auburn L. 1.	1	4·56	4·31	4·12	Length, 55 centimetres. Four tests on each hair.
" "	2	5·18	6·18	3·12	
" "	3	5·12	4·12	4·00	
Average ..		4·95	4·87	3·75	
Auburn-Brown L. 2.	1	5·81	4·87	3·75	Length, [illegible] centimetres. Four tests on each hair.
" "	2	6·06	4·12	4·18	
" "	3	6·12	4·62	3·62	
Average ..		5·99	4·53	3·85	
Total average } Silk ..		3·03	2·88	2·70	The method of testing is shown in the figure, p. 26
Total average } Hair ..		4·79	4·30	3·71	

Taking the strain to which a strand of silk sterilized in oil may be subjected to without danger of breaking at 2 ounces, and the number of stitches placed in uniting the ends of a carotid artery of a medium-sized dog at 20 stitches, since there are really two strands

to support the load on each stitch, the total safe load that the stitches could carry would be 80 ounces. The actual load thrown upon the stitches, obtained by multiplying the cross-sectional area of the vascular lumen by the maximum pressure of the blood, would not exceed 2 ounces. Indeed, such vessels have been tested by overloading them longitudinally, and they have been observed to give way to one side of the line of anastomosis. Using the entire thread of bead silk, as has been done—*e.g.*, by Watts—since the thread is composed of six strands, the combined strength of the sutures would be about six times that of the sutures consisting of single strands. In the case of human hair the breaking-point is considerably higher than for single strands of silk.

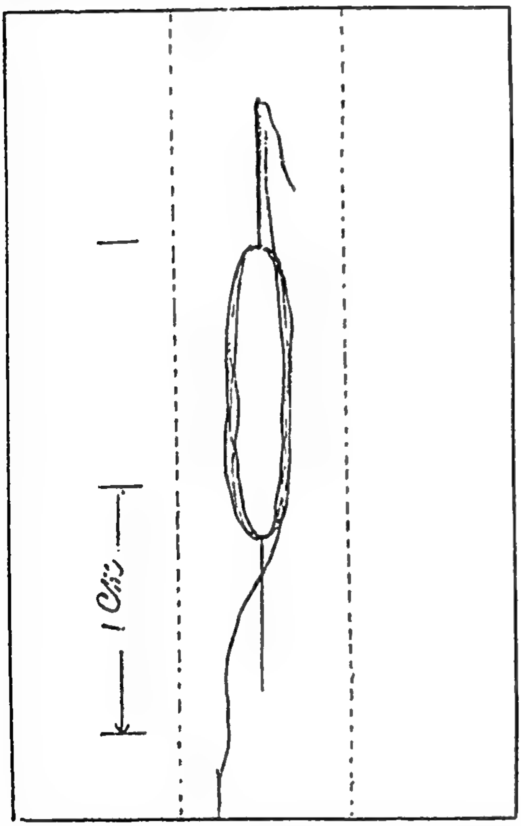


FIG. 20.—THREADED NEEDLE MOUNTED ON SLIP OF PAPER.
Dotted lines show where paper may be folded.
(*Journal of the American Medical Association*, 1910, liv. 349.)

Single threads should be tied securely into the eye of the needle, and one end clipped off to within ½ inch of the eye. The threaded needles are wrapped on small slips of paper to facilitate handling in sterilizing. Medium weight linen writing-paper is excellent for such slips, and a large supply can be quickly cut. It may be put in a small wide-mouth bottle or vial provided with a cork, and kept on hand if needles and thread are to be prepared for each operation. But a more convenient plan is to prepare a supply for some months at least, and after sterilization to put them away, so that they may always be ready. This may conveniently be done by folding the papers about the needle, as shown in the figure, to protect the thread and points of the needles, and inserting three together into small glass tubes containing heavy paraffin oil, and sealing the tubes and sterilizing by boiling. The oil may be previously rendered slightly antiseptic, but, if so, all excess should be

wiped from the needles and threads before using them on blood-vessels. If no antiseptic is used, the surplus of oil in the tube will come in handy for using on the blood-vessels to prevent drying during the time of the operation and to facilitate successful suturing.

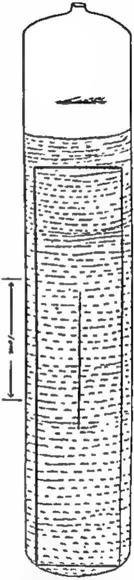


FIG. 21.—PAPER PACKAGE CONTAINING NEEDLE AND THREAD, PREPARED AS IN FIG. 20, IN SEALED GLASS TUBE CONTAINING STERILE OR ANTISEPTIC PARAFFIN OIL. (*Journal of the American Medical Association*, 1910, liv. 349.) Scale in centimetres.

If the needles and threads are prepared along with the other instruments for each operation, a plan that I have largely followed, an ordinary brass screw top microscope objective-box makes an excellent receptacle for holding the oil in which they are sterilized. Also by this method an abundance of sterile oil is assured without special thought or preparation. And the top of the box, set down like a cup, makes an excellent container for the oil used at the operation. Owing to its shape, it is not liable to be overturned, since it has a broad, flat base when thus used. Being small and compact, it may be placed close to the field of operation; and as it is shallow, the finger can be readily dipped into the oil. A disc of good quality of cork, which may be cut from one end of a stopper, should be snugly fitted inside of the top, the smooth surface of the disc being faced downward, so that, when the top is screwed on the box, a tight joint will be formed between the margin of the cork disc and the edgé of the side of the box. This is important to prevent the entrance of water into the box during sterilization. With the box about three-fourths full of oil, the papers bearing the threaded needles are dropped in, and the lid screwed on firmly. The box is then set in the solution of sodium carbonate in one corner of the instrument sterilizer, and boiled with the instruments. After sterilization is complete, the box should be removed (under aseptic technique) and the lid unscrewed, and both the box and lid set on the sterilized covering of the instrument-table. For if the

top should fit imperfectly, if left in the sterilizer after it began to cool, liquid might be drawn into it owing to the formation of a partial vacuum. Before being called for in the operation, the papers should be removed from the oil in the box, and the excess of adherent oil drained back into the box. Ordinary sterilized dissecting forceps are suitable for removing the needles from the box. The threads are then unwrapped by sterilized hands, and the needles and threads laid parallel on a smooth lint-free surface. The needles should not be withdrawn from the papers on which they are mounted, as the papers facilitate handling in passing to the operator. The nature of the surface upon which they are laid is important, especially as regards the absence of lint. Also a dark surface is better than a light one, as the threads are more readily seen, and therefore tangling and snarling is easier to prevent. A sheet of black oiled cloth, or a sheet of glass laid on a dark cloth, answer very well. Black suture material would, perhaps, be somewhat easier to manipulate than white, as in the bright light of the operating-room it would show more plainly. These latter considerations, though possibly appearing as trifling to the reader, are of distinct importance when the finest ligatures are employed.

Human hair in several ways fulfils the requirements of an ideal vascular suture material, as in homogeneity, fineness, strength, and smoothness. Perhaps the simplest method of preparation would be to sterilize the needles and hair in formaldehyde solution, and to apply sterilized oil just before using. We have employed this method, using 10 per cent. formalin, with perfect results. But hair may be sterilized in hot oil the same as silk. To be in the best possible condition for handling, the hair should not be kinked; therefore it should not be wrapped or curled tightly in its preparation.

Bull-dog forceps or serrefines are generally satisfactory for temporary occlusion of blood-vessels, and a sufficient number should be prepared for the operation to be performed, the number depending upon the nature of the operation. For example, in a simple end-to-end anastomosis but two are required. But several extra ones should be prepared, so that in case one is accidentally dropped upon an unclean surface, or for other unforeseen reason, the exact number deemed necessary should prove to be too small. The most useful size measures about 60 millimetres in total length. The blades are about 20 millimetres long and 5 millimetres broad. They taper slightly to the point, which is rounded. The outer surfaces are rounded and smooth, and the inner surfaces flat and transversely

corrugated. The corrugations number about two to the millimetre, and are shallow. The spring should be of such strength that, when the skin of the flexor surface of the forearm is grasped by the points, the points being separated by about 10 millimetres in applying to the skin, no sharp pain is produced in ten seconds. The blanching of the skin and the marks of the corrugations will disappear within thirty to sixty seconds after the removal of the forceps if the spring is of the proper strength. If the spring is set for too strong a pressure, this may be corrected by forcing them

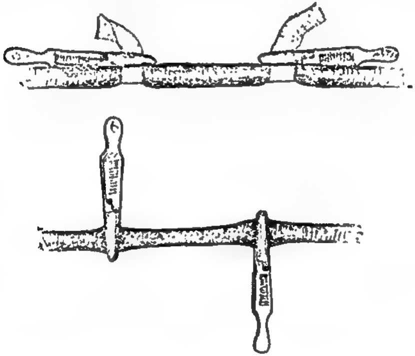


FIG. 22.—SHOWING TWO EFFICIENT METHODS OF TEMPORARILY OCCLUDING VESSELS FOR SUTURING.

together with a pair of pliers; or, if too weak, they may, of course, be made stronger by forcibly separating them.

On medium-sized blood-vessels, for example, the common carotid artery or external jugular vein of a 15-kilo dog—such forceps may be safely applied directly. But the vessel should be grasped near the point of the blades, as the pressure exerted by the spring is, of course, greater near the base of the blades. It is better, however, to either face the blades with muslin, fastening it to the blades by sewing or wrapping with a thread, or by passing a narrow thin tape or strip of cloth about the vessel at the point to be occluded, and while exerting gentle traction upon the two ends, in order to

will then neatly and safely constrict the vessel against the end of the tube. Tension on the ligature may be maintained by grasping both strands of the ligature with serrefines or other light forceps, the blades of which are placed crosswise the end of the tube and in contact with it. After placing the tube in position, the wound may be closed about it, as it can be withdrawn, and the ligature cut and withdrawn in an instant. If necessary, a single stitch in the skin will then finish closure of the wound, or a metallic skin-clip may be used. But if a tube of proper size is employed, no such suture will be necessary, as the tissues will, in virtue of their elasticity, fill the space previously occupied by the tube.

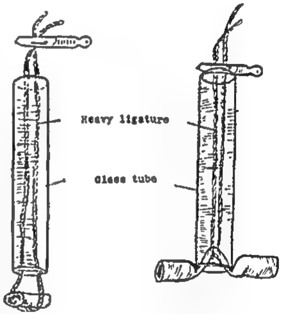


FIG. 23.—SHOWING METHOD OF TEMPORARY ARTERIAL COMPRESSION BY MEANS OF A SNARE.

For aid in handling the tissues of the blood-vessels and the needles and thread in suturing, two light, slender, curved, or one curved and one straight, dissecting forceps are invaluable. The points should be fine, but not sharp. They are the type of forceps used in making the finer dissections in studying the anatomy of frogs and such animals, and they may therefore be obtained from any first-class biological laboratory supply-house.* A pair of small scissors, also used for such dissections, are very useful for working on blood-vessels. The blades are sharp-pointed and keen, making a clean cut, with little crushing. Two pairs of medium straight surgical dissecting forceps, a medium pair of ordinary surgical scissors for general dissection, and a pair of fairly large scissors for rougher work, such as cutting cloth, are prepared. Two surgical knives of the narrow, hollow-ground, straight-bladed (spear-point) English form; six pairs of medium hæmostats; six pairs light hæmostats (Halsted mosquito); and one straight and one curved, slender-jawed, heavy hæmostats, are also prepared. Two large,

* The form sold by Bausch and Lomb, of Rochester, New York, is excellent.

two medium, and two small curved triangular-pointed suture needles complete the list of surgical instruments generally employed for operations for suture of blood-vessels. The instruments are sterilized by boiling in dilute sodium carbonate solution for at least ten minutes. They are removed immediately from the sterilizer, and assorted and arranged on the instrument-table. Any excess of solution remaining on them after cooling for a short time is removed with a sterilized cloth. The use of much sodium carbonate in the water, to prevent rusting, is to be avoided, as it is unnecessary. And if much of the salt is used, the instruments will be so heavily coated with it after they have dried that they will have to be gone all over with a cloth in order to be in good condition for the operation, which is bad both from the standpoints of time and of asepsis.

Ligature and ordinary suture material may be prepared, or the commercial, aseptically prepared, may be used. Quite a number of commercially prepared catguts have been used, and they have all been satisfactory. One of the most satisfactory, owing to its pliancy, is that prepared under a method published by Dr. Willard Bartlett. A slowly absorbable gut should be used, especially in the outer tissues. For example, if an extensive abdominal opening in a cat is closed with a quickly absorbable gut, the chances are very great that the wound will open. As to size, No. 2 is the most generally useful, but a size smaller may be used on cats or other small animals with good results. A half-dozen 8-inch medium twisted or braided silk ligatures and a dozen fine twisted silk ligatures are prepared along with the instruments. They may be simply boiled in the carbonate solution with the instruments, but as a rule I put them in the box with the needles and thread, as they handle nicely when taken from the oil, and the results are good. In case they are boiled in the carbonate solution, they are rinsed with sterilized 0·9 per cent. sodium chloride solution before being used. Whether this leads to better results I do not know, but since the sodium carbonate impregnation is an untested factor with us, I prefer to rinse with the sodium chloride, even though there is no reason for anticipating any observable difference in the results.

The suture and ligature materials are arranged on the table along with the instruments, if all are prepared at the same time. In the case of commercially prepared gut, the technique ordinarily employed by surgeons is followed, which varies somewhat with different forms of gut. But sufficiently explicit directions are

usually found upon the wrapper in which it comes to enable the operator to use it properly.

Gowns, table-covers, operating-cloths, towels, napkins, absorbent and plain cotton, gauze, cotton-gauze sponges, oiled silk, roller bandages, and the like, are so nearly of the ordinary surgical type that very little description is necessary.

A list of cloths and materials prepared for the operation is as follows: Four gowns; one heavy muslin cover, 24 by 24 inches, for instrument-table; four heavy muslin covers, 26 by 36 inches, for operating table; one heavy muslin cover, 32 by 50 inches, for dressing-table; four, 20 by 30 inches, heavy muslin cloths for covering animal; one dozen, 16 by 32 inches, soft hand-towels; half a dozen heavy hand-towels; one dozen, 14 by 14 inches, soft napkins; one roll absorbent cotton; one roll plain cotton; two dozen cotton-gauze sponges, size hen's-egg; 1 yard gauze; three pieces oiled silk, 6 by 4 inches; one 5 yard 2-inch rolled bandage; 1 yard heavy unbleached muslin for making tailed bandage for completing dressing. A bottle of powdered boric acid is placed conveniently for dusting the wound before dressings are applied.

The gowns, operating-cloths, and dressings are sterilized in live steam for twenty minutes or more at a temperature of at least 120° C., after which they are removed, and spread out on the table placed in the operating-room for that purpose.

Preparation of Animal.

Animals in good condition should be selected for best results. If very dirty, they should be washed the day preceding operation in a warm room in warm water, using a mild toilet soap. The bath should occupy a short period, and the animal should be quickly and thoroughly dried with towels, and then placed in a clean compartment in the hospital. The purpose of the bath is for the removal only of the excess of dirt, and it is not to sterilize or render the coat aseptic. Only the hands or a sponge are to be used, as harsher measures, as scrubbing with a brush, is very liable to lead to an irritated condition of the skin. After the bath the animal is supplied with clean bedding, excelsior, covered with a clean coarse bag, or other coarse cloth being excellent. A moderate amount of food and plenty of water is placed before the animal. Water, but no solid food, is given on the day of the operation.

The hours from 10 a.m. to 3 p.m. are the best for operating on account of light, but this depends to a large extent upon the

direction of exposure of the windows. When all is ready, the animal is brought into the preparation-room either by leading or carrying in a large coarse bag. In general, the most satisfactory method of handling animals in taking them from place to place is to put them in such a bag. The mouth of the bag is tied so that when laid upon the floor the animal cannot get out.

Anæsthesia is quickly and humanely produced in the following manner: One or more heavy towels are spread upon the floor; a flake of cotton batting, as large as the two hands, is then placed on the towel about one-fourth of the length of the towel from one end. The towel is then folded in the middle, so that the two ends come together. The dog, having been removed from the bag, is then stood with its nose over the towel. The anæsthetist kneels or squats to the right of the animal, and grasps the skin of the nape of the neck gently with his left hand. An assistant takes position to the left of the animal, and grasps both fore-legs just above the feet with his left hand, and both hind-legs similarly with his right. The anæsthetist then pours ether upon the towels at the point above the centre of the flake of cotton. Enough ether is poured on to saturate the cloth and cotton thoroughly for a space as large as the hand. The ether-can is quickly set aside, but in convenient reach, and both hands of the anæsthetist placed firmly about the animal's neck, and the head laid upon the towels so that the nose lies over the centre of the ether-saturated portion. The assistant at the same time draws the legs from under the animal, so that it is laid upon the floor gently and quickly. The anæsthetist instantly removes the right hand after the animal is laid down, but the left is held firmly on the neck, pressing downward and forward so that the fingers are under the angle of the jaw, and therefore out of harm's way. With the right hand the towels are thrown over the throat, and pulled well back on the neck, and held by placing the hand against them, and thus grasping the neck with the thumb pressing behind the left ear, and the index-finger behind the occiput. The left hand is then quickly snatched backward and out from under the towel, and replaced in its former position, only this time on the outside of the towel. The thumbs of the two hands come together behind the occiput, while the fingers encircle and gather in and firmly hold the towel beneath the animal's throat. The assistant keeps the fore- and hind-limbs well separated. By this method practically all excitement of the animal is avoided, and the period of struggling is very brief. Indeed, the animal usually is com-

pletely anæsthetized in less than one minute, and the method is very safe.

As soon as the animal is anæsthetized, it is placed upon the drain-board in connection with the sink, and the field of the operation rubbed with liquid soap and shaved. A few strokes of a well-sharpened razor properly applied—that is, with a sliding stroke from the point toward the heel—will remove the hair from a large area, and leave the skin in excellent condition. Previous clipping of the hair is unnecessary. The stroke of the razor should always be in the direction of the hair. Also traction should be exerted on the skin, so that it may be stretched under the edge of the razor. This is conveniently accomplished by placing the hand on the skin back of where the razor is started.

After the hair is removed, the shaved area is washed with more of the surgical soap solution and water, using a cloth or cotton sponge, and all excess of moisture removed first from the shaved surface, which is uppermost, and then the surrounding portion of the coat. A little strong alcohol (95 per cent.), or alcohol-ether mixture, is then used on the shaved area to remove fatty substances and to aid in sterilizing, and this is followed by a pad of absorbent cotton saturated with 1 in 1,000 bichloride solution, the pad being applied to the whole of the shaved area, and pressed lightly against the skin.

Looped tapes having been affixed to each leg immediately above the ball of the foot, the animal is carried in to the operating-room and placed upon the table, which is covered with a waterproof cloth, to protect the enamelled top from the action of alcohol which is subsequently used, and to keep the animal from undue cooling from direct contact with the table-top. The tapes upon the feet are then fastened in the holes of the frame of the table-top and suitable sand bags in waterproof covers placed about the animal to keep it in position. One placed longitudinally on either side of the thorax and one transversely under the neck suffice; but if operating upon the abdominal vessels, one such bag should be placed transversely under the back below the point of operation. A rubber hood is then placed over the head and firmly fastened around the base of the neck, but care must be taken not to make it so tight as to interfere with either circulation or respiration. The extremity of the hood is tightly fastened to the margin of a metal funnel, so that by connecting the stem of the funnel with an anæsthetic bottle by means of a piece of flexible tubing the administration of ether becomes almost automatic. Or in place of the

hood a tube may be passed through the larynx into the trachea and similarly connected with the ether bottle (see p. 306). The tube is held in place by a coarse, soft ligature, tied first about the shank of the tube and then around the lower jaw of the animal behind the canine teeth. The tube is easily inserted into the larynx. In a good light, the neck is moderately extended and the tongue grasped with a cloth and pulled forward. This raises the larynx and brings the glottis plainly into view if the jaws be separated and the head held towards a window, so that light may shine down the animal's throat. It is well to insert

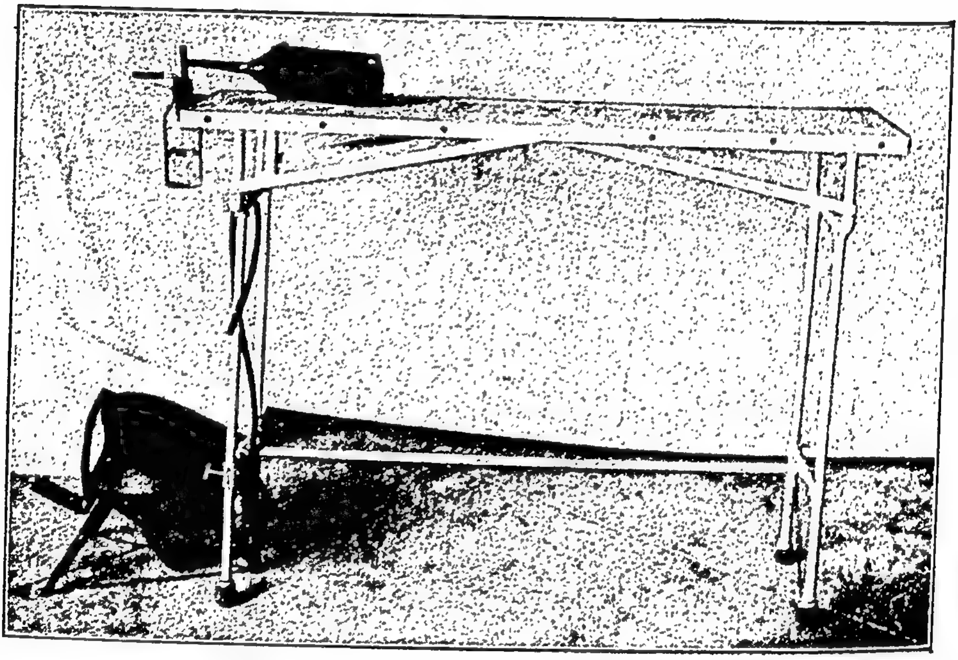


FIG. 24.—OPERATING-TABLE, WITH ARRANGEMENT FOR GIVING ANÆSTHETIC. ALSO BELLOWS FOR GIVING ARTIFICIAL RESPIRATION, IF REQUIRED, IS SHOWN.

a piece of soft wood in the corner of the mouth on one side between the jaw teeth to prevent accident while inserting the tube. The laryngeo-tracheal tube is in several respects superior to the hood method of giving an anæsthetic, especially on small animals; for not only is the surgical field less encumbered—especially in operations upon the neck or about the head—but the lungs are in unobstructed communication with the outside during the entire course of the operation, and no obstruction can be produced, as by the accumulation of mucus in the pharynx or the walls of the larynx coming together, which sometimes are serious complications in general anæsthesia; nor can gastric liquid or other material enter the lungs

in case of vomiting, as may happen under other methods. Finally, in case of respiratory failure, efficient artificial respiration may

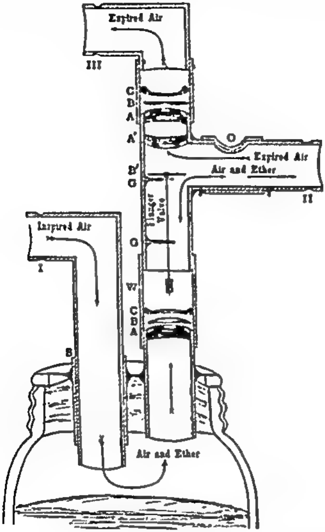


FIG. 25.—RESPIRATION VALVES.

I. Entrance for air into anæsthetic bottle. S, Collar in which tube slides for adjusting the amount of ether.
II. Connection for laryngeal or tracheal tube. O, Opening in tube and movable collar for adjusting the admixture of air.
III. Outlet for expired air. By connection with gasometer the amount of expired air can be measured; or by connection with spirometer, the expired air can be measured and collected for analysis. A marker may be connected with the spirometer, and arranged to show on a moving surface the amount of expired air.
A, Valve seat; B, valve disk; C, valve stop; B', valve to close the opening at A' when artificial respiration is given by means of rhythmic or positive pressure through I; W, weight for regulating the action of valve in forced artificial respiration.

immediately be given, and at such times seconds are precious. But in using this method too large a tube should not be employed, and reasonable care should be exercised to avoid straining or injuring

the larynx in any manner. I have used the method many times, and have yet to observe a single bad after-effect attributable to it.*

A pair of bellows or a compressed air-supply are available for use in operations necessitating the opening of the pleural cavities or for giving artificial respiration as occasion may demand.

The operation itself is carried out with the aid of an anæsthetist, an assistant operator, and an instrument and dressing passer. All are clothed in sterilized gowns, and the heads of the operators are covered by caps made from towels by tying two opposite corners together behind the head and folding down the other corners and pinning into place. Gloves are not worn, but the hands and fore-arms of all but the anæsthetist are thoroughly washed, sterilized in bichloride of mercury solution and alcohol, and then rinsed in sterilized water.

The anæsthetist is provided with a stool and placed at the head of the table. In addition to regulating the anæsthesia he handles the animal, as may be necessary during the operation, by placing his hands beneath the sterilized coverings. Also he keeps written notes of the operation. The operator stands to the right of the table, and faces the anæsthetist. The table is so placed that the side-light comes from the operator's side of the room. The assistant stands on the other side of the table, so he is between the operating- and dressing- and instrument-tables. The instrument and dressing passer is stationed close to the assistant and within easy reach of the instrument- and dressing-tables. The bichloride dressing is then removed from the shaved operation field and the area sponged with alcohol, and a thin pad of absorbent cotton saturated with alcohol applied to the shaved surface. Supposing that the operation is to be ligation and division of both common carotid arteries and anastomosis of the central end of the right to the peripheral end of the left, the shaved area will extend from the cricoid cartilage above to about an inch below the anterior end of the sternum, and well down on either side of the neck. The sand-bag, previously placed transversely beneath the neck, should cause extension of the neck backward below the point selected for division, and any such adjustments necessary are made by the anæsthetist, who carefully avoids touching the shaved area. The trunk of the animal is now covered by at least two thicknesses of heavy sterilized cloth, which

* For illustrated account of method of giving anæsthetic to animals, see *Jr. A. M. A.*, 1911, lvii. 887.

extends over the edge of the table. The head down to the upper margin of the shaved area is covered by similar cloths or towels, placed transversely so as to cover the entire anterior end of the table. Then a heavy towel is placed longitudinally on either side of the neck, so that the inner edges come together in the mid-line both above and below the shaved area. The edges of these towels are then grasped together with the underlying cloths, and fixed with forceps (Pean's are good, owing to the spring of the blades) about an inch both above and below the margins of the shaved area. The cotton pad is then removed from the shaved area, and after rinsing the hands again in the antiseptic solutions and water, the operation itself is begun. The animal is, of course, completely anæsthetized, which condition is maintained until after the wound is closed.

With a knife held between the tip of the thumb and fingers, so that the cutting edge is almost parallel with the surface of the skin through which the incision is to be carried, and with the skin fixed to prevent it sliding and following the knife, which is accomplished by pressing with the thumb and forefinger of the left hand at a point on a level of and to either side of the anterior point of the proposed incision, the skin is divided in the mid-line by a single, firm, continuous stroke of the knife, from about an inch below the cricoid cartilage to near the upper end of the sternum. If properly made, the skin and adherent subcutaneous tissues will be completely divided, and a very slight amount of hæmorrhage will occur. But however trifling the hæmorrhage, it is lightly stroked with a dry cotton-gauze sponge and, if need be, lightly compressed until the wound is dry. While this is being done the anterior and posterior extremities of the incision are grasped by Pean or other strong forceps together with the inner edges of the longitudinal and laterally placed towels, and skin and towels fixed together. The handles of the forceps in both cases extend away from the points of the incision. Next, two or more similar forceps are made to grasp and fix the skin and edges of the towels together at opposite points along either side of the wound, with the handles placed outward, so that nothing is exposed but the structures appearing in the bottom of the wound. With a few light strokes of the knife the inner margins of the sterno-hyoid muscles are exposed, and the anterior median vein, lying between them, comes into view. With a pair of blunt dissecting forceps in either hand, and using them as blunt needles with the blades closed, the inner margins of the sterno-hyoid muscles are

separated, the median vein being left attached to the one to which it seems most tightly adherent. Venous branches of any considerable size, running to the opposite muscle, are then crushed or stretched until they are divided, and any hæmorrhage controlled by applying hæmostats to the bleeding-point. Bleeding from these vessels is usually slight, and when the hæmostats are removed, as a rule no further escape of blood occurs from the divided vessels. The tissues down to the anterior surface of the trachea are then separated by means of the blunt dissecting forceps, used as before, until a space large enough to admit the tips of the index-fingers is made. The fingers are inserted back to back and slightly flexed so that the tips hold in the tissues. Then, by careful but firm traction, with the fingers acting in opposite directions, the tissues are pulled apart until the trachea is exposed for nearly the whole length of the wound. Working first on one side and then on the other, in a similar manner the carotid sheaths are exposed. Notwithstanding the extensive separation of tissues thus quickly accomplished, not a drop of blood need be shed. The forceps holding the skin and towels together at the sides of the wound may now be released and reapplied to also include the tissue bordering the inner margins of the sterno-hyoid muscles, thus exposing more effectively the deeper structures; or, without disturbing the forceps holding the skin and towels, additional forceps may be used to fix the margins of the muscles to the towels, which is perhaps a somewhat better procedure if sufficient forceps are on hand. Each carotid artery is in turn picked up by passing the point of the left index-finger beneath it, and, if the operator be sufficiently expert, the artery is exposed and freed from the internal jugular vein and vagus nerve by delicate use of the knife. Or closed blunt dissecting forceps may be used to separate the artery. It is strongly adherent to the nerve, and care must be taken to avoid straining or injuring either of the structures.

After the arteries are freed for the entire extent rendered accessible by the wound, they are grasped and crushed with heavy, tapering-jawed, hæmostatic forceps, the right high up so as to give a long central end after division, and the left low down so that it may have a long, free peripheral end. Strong, but not very coarse, silk ligatures are then passed about each artery in turn, and the vessels firmly and securely ligated, in the case of the right artery above, and in the case of the left artery below, the hæmostatic forceps. The ends of the ligatures are then cut off within $\frac{1}{8}$ inch of the vessels.

A pair of bull-dog forceps, previously tested as to strength, and preferably having cloth-covered blades, are applied to each artery, in both cases at as great a distance as possible from the corresponding hæmostatic forceps previously applied.

The vessels are then transversely divided with a single, firm rapid movement of the blades of a pair of small, keen scissors, the line of division in each case being within a few millimetres of the hæmostatic forceps. After dividing one vessel, it is stripped several times between the balls of the finger and thumb, from the serrefine

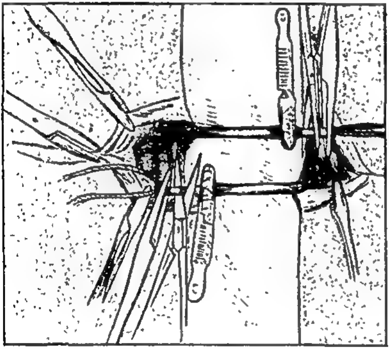


FIG. 26.—END-TO-END ANASTOMOSIS.

Carotid arteries exposed, permanent ligatures and temporary hæmostatic forceps applied, with scissors in position, to show preparation of vessels for anastomosis of the central end of the right to the peripheral end of the left. Drawing from photograph. Through an inadvertence the temporary clamps appear too near to the scissors. See following figures.

to the cut end, over which a dry cotton-gauze sponge is held. After all excess of blood is thus removed, a little oil is applied to the end of the vessel with the finger. The second vessel is then divided and treated in exactly the same manner. The hæmostatic forceps on the ligated ends of the vessels are now removed, and the wound wiped out gently with a dry sponge.

A strip of waterproof material, having a lint-free surface, and sufficiently wide to cover the floor of the wound, is placed transversely in the wound, and the ends of the vessels to be anastomosed

are brought close together on its upper surface. Oiled silk or other similar cloth, or rubber-coated cloth, serves well for this purpose. If the material be black the threads used for anastomosis may be more easily seen, and it will be less fatiguing to the sight.

Anastomosis of the Vessels.

The operation of anastomosing is now begun. The end of each vessel is examined in turn, and the loose outer sheath is slipped back for a few millimetres from the end. It may be that the end of the vessel is covered by this sheath, in which case the excess is removed by grasping the loose tissues over the end of the vessel with the ball of the left thumb and forefinger, and, while exerting light traction, to snip off the excess with sharp scissors. The outline of the end of the vessel will show plainly, and the cut is to be made distal to it. When this is done, the outer loose tissue remaining is pushed back from the end of the vessel as before described. The fingers alone are used for such handling of the vessels. After the ends of both vessels are thus prepared and inspected to see that they are cleanly and evenly cut, and that they are free of blood, either liquid or clotted, and any such undesirable conditions remedied by the methods already described, the operator lightly oils his fingers, which should be clean and dry, and then begins placing the three fixing sutures. The vessels are examined to see that they are not twisted, and then picking up the central end of the right artery, a needle carrying a vascular suture is thrust through the middle of the posterior wall, within ½ millimetre or less of the free cut surface from without inward, taking care to penetrate all the coats, including intima. After penetrating the intima, the point of the nee

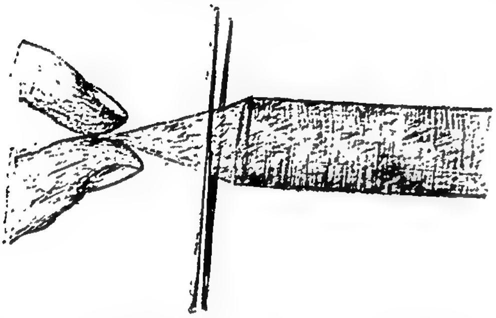


FIG. 27.—SHOWING METHOD OF REMOVING EXCESS OF PERIVASCULAR TISSUE FROM AN ARTERY AFTER DIVISION, PREPARATORY TO ANASTOMOSIS.

(Diagrammatic.)

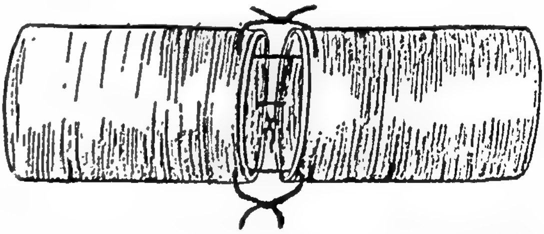


FIG. 28.—SHOWING POSITION OF PRIMARY FIXING SUTURES IN END-TO-END ANASTOMOSIS OF BLOOD-VESSELS.

is directed anteriorly so as to avoid the opposite side of the vessel wall. If, by light traction, the assistant can bring the ends of the two vessels close together, the point of the needle is then directed dorsally, and made to penetrate the corresponding points in the mid-line on the posterior wall of the peripheral end of the left artery, from the intimal surface outward. The point of the needle is then grasped between the left thumb and forefinger, and the ligature drawn about halfway through. A single knot is then tied in the ligature, so that but little traction may be exerted on the

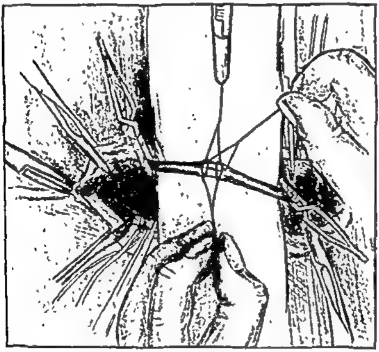


FIG. 29.—APPOSITION OF ENDS OF DIVIDED ARTERIES BY MEANS OF STAY SUTURES, PRELIMINARY TO CONTINUOUS STITCHING TOGETHER.

(Drawing from a photograph.)

ends of the vessels, and the free ends are held by the assistant, who draws them toward the left side of the animal, which produces a quarter twist in both ends of the vessels. The operator now places the second fixing ligature, which, being one-third of the circumference away from the first one, will come almost on the uppermost point on the circumference of the vessels as they are being held by the assistant. The direction of the needle is the same as in the first instance, but the ligature is more easily placed as the vessels are in a more favourable position. A pair of light, tapering forceps may now be used by the left hand to press the tissues back as the needle

is thrust through. This is done not by grasping the tissues, is to be avoided, but by pressing against the tissues with the s the closed blades. As soon as the point of the needle is th the walls of both vessels far enough to be grasped, it is seized the forceps and drawn through, and the ligature tied loosely, the case of the first one; but if the cut edges of the vessels m brought together with little or no resistance, the two ligatures be firmly tied before placing the third one. The assistant drops the end of the posterior ligature, and the operator pull ends under the vessel to the right side of the neck by reac beneath the vessel with a pair of light, curved forceps, and pa the curved surface about the ligatures and drawing them ur neath and out from the vessel. The assistant now holds the ligature, which is also the posterior, but which is now drawn tc right side of the n in the fingers of right hand, and second ligature, wl is the left side of vessel when the vesse in its natural posit in his left hand, exerts very gentle firm, steady tracti upon the vessel, wh should not be more tl is necessary for slightly lifting the point at which the anas mosis is being made from the waterproof covering over the floor the wound. The operator then places the third and last fixi suture through the margins of both ends of the vessel, at a poi equidistant from the first and second sutures, using the same tec nique as in the placing of the second. The ligature is then tic which ends this stage of the operation.

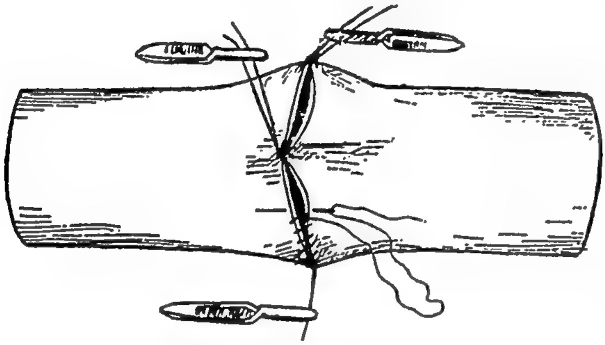


Fig. 30.—Showing Tension Sutures and Continuous Stitches partially placed in the Union of the Ends of Blood-Vessels.

The operator next grasps both strands of the posterior ligatu and separates the two ends. The needle is used for sewing tl edges of the vessels together and he takes it in the fingers of his rigl hand, while the other end of the ligature is held by the fingers of h left hand, and by means of it he exerts gentle traction against tl ligature placed in the right side of the vessel—the last one to l placed—both ends of which are grasped by the fingers of the lel hand of the assistant. With his right hand the assistant manipu

lates a pair of light, tapering, curved or straight dissecting forceps, and not only presses against the tissues of the blood-vessel as the operator thrusts the needle through the walls, but as soon as the needle is through to the extent of about one-third of its length he grasps the bar of the needle with the forceps near the point of exit from the tissue and pulls it through. The operator places the stitches through the margins of the walls of the cut ends of the vessel, as in the placing of the fixing sutures. The stitches are placed so that inside the vessel the thread will be at right angles to the line of anastomosis. Care is taken to actually see in every case

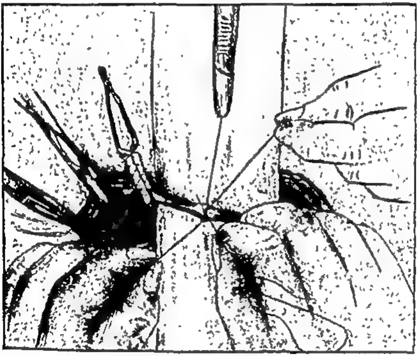


FIG. 31.—STITCHING BETWEEN STAY SUTURES SHOWN IN FIG. 29. The needle is turned *obliquely for purpose of better illustrating. (Drawing from a photograph.)*

that the stitches include all the coats of the walls of both vessels and that no loose outer tissue gets between the cut surfaces of the vessels. As soon as the needle is drawn through by the forceps of the assistant, it is immediately seized again and the stitch drawn until all slack is removed. The next stitch is then placed in the same manner, and the process repeated until the doubled ligature held by the assistant is reached. The suture is then tied with a double knot with the doubled fixing ligature. A pair of serrefine forceps are then attached to the end of the posterior ligature that has been held by the fingers of the left hand of the operator, after

which the end of the ligature is released. The main purpose of the serrefine, is to act as a weight so that when traction is made upon the other two fixing ligatures by the operator and assistant, the vessel, being not only stretched between the ligatures transversely, but lifted up so that the serrefine is at least in part suspended, by the traction of the serrefine at the point of anastomosis, is caused to assume a triangular form. Thus the lumen of the vessel is held open and less care is necessary to avoid accidental inclusion of the wall opposite to the point where suturing is being performed from being injured or included in the stitch.

The operator then, with the fingers of the left hand, grasps both ends of the fixing ligature previously held by the assistant, which has been knotted with the suture, and the assistant similarly grasps the two strands of the fixing ligature remaining free—that is,

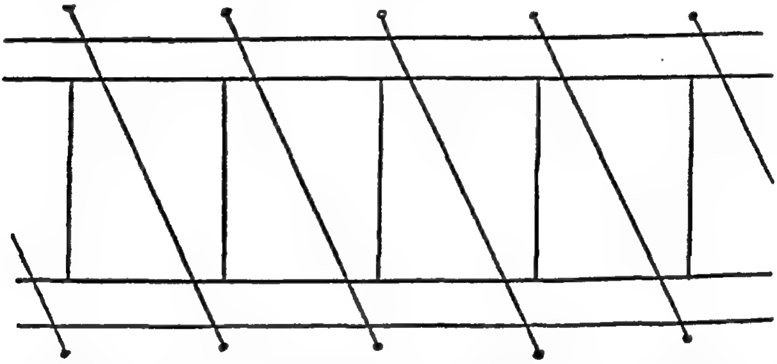


FIG. 32.—DIAGRAM TO SHOW DIRECTION OF CONTINUOUS SUTURE ON OUTSIDE (OBLIQUE) AND INSIDE (TRANSVERSE) OF A BLOOD-VESSEL.

the one placed in the left wall of the vessel—and the edges of the vessel between the ligatures are sutured by continuous stitching as before, and the suture is knotted to the ligature held by the assistant in the same manner as before practised. The strands of the ligature held by the operator are then released to a pair of serrefines, which may be taken from the posterior ligature. The ends of the fixing ligature held by the assistant are then grasped in the usual way by him, and by means of curved forceps he draws the end of the posterior ligature beneath the vessel to his side of the neck, and grasps it as he previously grasped the fixing ligature. Th third and last line of sutures is then placed, and the suture knotte to the end of the suture held by the assistant. The suture and al the ligatures are then snipped off with keen scissors at a distance o 1 to 2 millimetres from the wall of the vessel. The outer loose coa on either side of the line of anastomosis is then gently stripped in th

direction of the line of anastomosis, which it may or may not cover, depending on the amount removed in the preparation of the vessel, the degree of traction on the vessel, etc. This completes the anastomotic operation proper.

The distal serrefine on the artery is now opened and the blood allowed to flow into the occluded portion of the vessel from the cephalic end. A little blood will escape from the needle holes on either side of the anastomosis, but if on examination of the entire circumference of the vessel at this point no considerable leakage, due to faulty approximation or incomplete drawing together of the cut edges, is observed, the serrefine is removed, and a dry cotton-gauze sponge pressed firmly over the point of suture. The serrefine on the central portion of the artery is immediately removed, and the full carotid pressure allowed to enter the vessel. The sponge is then cautiously raised and the line of union examined for free hæmorrhage. If none is observed, the sponge is replaced and light pressure on the anastomosis maintained for one minute. The pressure should not be sufficient to entirely occlude the lumen of the vessel, but it should be great enough to retard the circulation somewhat so as to favour the more rapid deposit of fibrin in the needle holes and crevices between the intimas of the two portions of the vessel. The sponge is then removed and the vessel presents a dry, smooth external surface, and the line of anastomosis is almost invisible. Should a little oozing yet occur the sponge is reapplied with gentle pressure until the leakage has ceased. In the event of a *freely* spurting point occurring, the index-finger of the left hand is inserted beneath the line of anastomosis, and the vessel raised somewhat and rolled on the ball of the finger until the leaking-point is brought uppermost. It is then carefully located, and a stitch placed so as to embrace the outer coats of the vessel on either side of the opening, and the suture tied so as to close the opening; or two or three continuous stitches are placed, and the ends of the ligature gently drawn upon so as to draw the tissues together, and the ends of the ligature cut off near the surface of the vessel, no tying being necessary. The loss of blood will immediately stop if the work has been done properly. If the escape of blood is so great as to interfere with correction of the defect, and if compression of the vessel central to the point with the ball of the thumb and the finger inserted under the vessel is inadequate the assistant then aids by compressing the vessel above with the right thumb and forefinger; or serrefines may be again placed upon the

vessel. In placing such stitches care must be exercised to avoid penetrating or injuring the opposite wall of the vessel with the needle, and it is for that reason that the intima is not to be included in the suture.

The vessel is now seen to be round and full and strongly pulsating. It courses obliquely across the trachea, from the right to the left side of the neck. Its colour will depend upon the degree of anæsthesia, so if the arterial blood is venous-hued it will present a bluish or purplish appearance, while if the blood is more nearly normal arterial it will be of a redder hue.

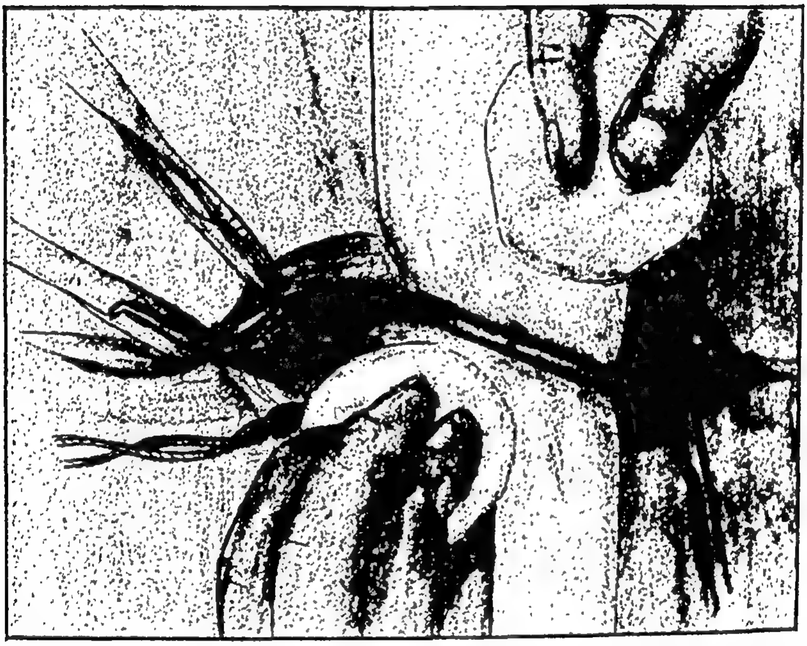


FIG. 33.—END-TO-END ARTERIAL ANASTOMOSIS SHOWN IN PRECEDING FIGURES COMPLETED, AND CIRCULATION RESTORED.

(Drawing from a photograph.)

The next step in the operation is the closure of the wound. This is done by means of a curved suture needle, bearing a single strand of medium-size catgut, which is tied into the eye to prevent unthreading. The wound is now wiped out, either with a dry sponge or one moistened in 0·9 per cent. sterilized sodium chloride solution; but if the solution is used, all excess is removed by sponging, the tissues being left dry or only slightly moist.

Next the inner margins of the sterno-hyoid muscles are released from the retaining clamps and brought together. Beginning below, the edges of the muscles, including the dorsal aponeurotic tissue, are sutured together with the curved needle and gut. The first

stitch is firmly tied, leaving the free end of the ligature several inches long. The operator then grasps the free end of the ligature in his left hand and exerts sufficient traction upon it in the posterior direction to slightly stretch the tissues along the line of suture and bring them closely together in the mid-line. He then quickly sews the two edges together, using continuous sutures, placed sufficiently close to hold the tissues firmly and continuously together. When the first stitch after tying is placed, he releases the free end of the ligature to the left hand of the assistant, who continues the traction upon it as previously described. The operator pulls each stitch or each second stitch firmly into place, and while the succeeding stitch or pair of stitches is being placed, gentle tension is maintained with the left hand upon the ligature between the preceding stitch and the needle, but near the former in order that no slacking of the suture already in the tissue may take place; or such tension may be maintained by the right hand of the assistant. In any event, either the operator with his left, or the assistant with his right hand, depending upon the one that is free, grasps the tissues between the thumb and forefinger slightly ahead of the needle, and presses them firmly together from side to side, thus insuring evenness in the stretching and aiding the penetrating of the tissues by the needle by fixing them. When the last stitch in the anterior end of the suture line is placed, the remaining ligature is drawn through only a few inches, and the slack ligature between the last two stitches is doubled together and firmly knotted with the end bearing the needle. The ends of the suture are all then cut off within ¼ inch of the surface of the tissues. The anterior exposed tissues of the neck are then wiped with a sponge moistened with salt solution, after which the remaining unsutured tissues, divided by subcutaneous incisions, are stitched together in the mid-line as in the manner just described. The remaining exposed tissues to and including the edges of the skin are wiped with a sponge moistened with salt solution, and the side retaining clamps released Using a heavier or more slowly absorbable gut, the skin is now sutured in the same manner, excepting that the stitches are placed more closely together and the clamps at either end of the incision

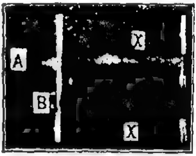


FIG. 31.—ANASTOMOSIS OF—A, ARTERY TO ARTERY; B, VEIN TO VEIN; SHOWING EXTERNAL SURFACE AT END OF OPERATION.

are removed. The line of union of the skin is now very firmly rubbed from above downward with a sponge well-moistened with alcohol. Any projecting subcutaneous tissue is thrust into the suture-line by means of blunt dissecting forceps. Excess of alcohol is removed, and the shaved surface of the skin sprinkled with powdered boric acid or iodoform, but preferably the former, and a thin pad of absorbent cotton, about 2 inches wide, applied over the line of skin suture. The anæsthetic has now been discontinued and the re-

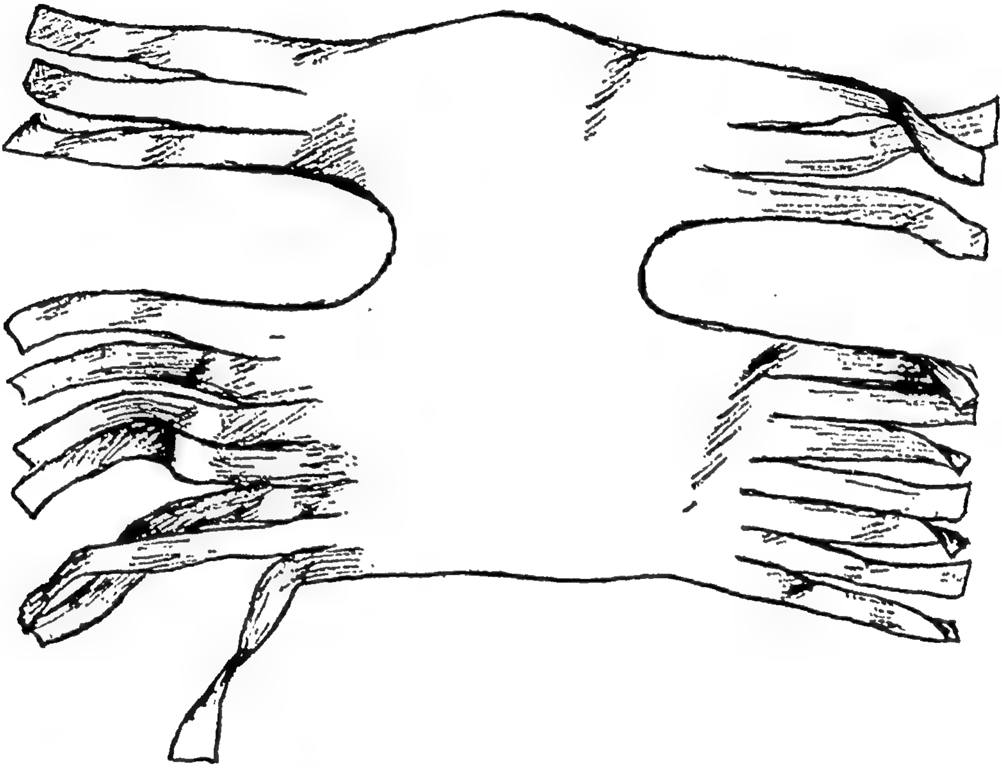


FIG. 35.—TAILED BANDAGE, FORMING OUTERMOST DRESSING FOR NECK OR TRUNK.

The rounded slots are for the fore-legs. Each pair of tails is knotted together over the dorsal mid-line, and adjacent ends of each pair are then knotted together. This form of bandage has been employed by the writer since 1903 with entire satisfaction.

mainder of the dressings are rapidly but carefully applied. These consist next of a thick pad of absorbent cotton of the proper length and width to embrace the whole of the neck, the lap being on the back of the neck. It is applied with the animal lying on its left side, the tapes having been removed from the wrists and ankles. A similar but heavier and somewhat larger pad of untreated cotton is next applied over the absorbent cotton, and it is long enough to encircle the neck two or three times. The cotton is now encircled with a firmly but not too tightly applied roller bandage, which is

fastened at two or three points along the dorsal mid-line with small safety-pins. A tailed bandage of suitable size should be at hand, but if such is not the case, one may be quickly made from a piece of heavy muslin. It is fitted over the dressing, and the ends of each pair of tails are tied in a single knot. After it is seen that the bandage fits snugly all over, and that it does not press too tightly at *the edges, especially where it passes between the fore-legs, the knots* are securely tied. The free ends of each pair of tails are then separated and laid in opposite directions, and each end is then firmly knotted with a member of the adjacent pair of tails on either side. When all are securely fastened, the ends are cut off within an inch of the knots, using heavy scissors kept for that purpose.

By thus knotting the ends of the tails together the dressing is made much more rigid and the divisions of the bandage are securely anchored together.

The dressing is now finished, and the nursing of the animal begins. At this time it will be coming out from under the influence of the ether, and before consciousness is fully re-established normal power of control of movements will be lacking, so it must be carefully watched to prevent its doing injury to itself. This may be done by having the attendant give his whole attention to the animal, it being placed on a dry, warm bed, in a well-ventilated but warm place, as by the side of the radiator in the preparation-room, several coarse sacks spread on the floor serving quite well for the animal to lie on. Another method, but perhaps not so good as the one above described, since the animal cannot be so closely watched, consists in placing the animal in a large, coarse-meshed bag, and suspending the bag so that it hangs freely in the air. Being unable to get a purchase on a fixed surface, the animal is unable to injure itself. After the animal has completely regained consciousness, which takes surprisingly little time in most instances, it is placed in one of the individual rooms in the hospital upon the raised screen bottom. A thick, soft cloth pad, which may consist of several coarse bags, is spread upon the screen bottom for the animal to lie upon, and a flat-bottomed vessel, partly filled with water, is supplied. The water vessel is set at some distance from the bed pad, preferably in a corner, in order to minimize the danger of accidental upsetting and wetting of the pad. *No solid food is given until the following* day, when the animal is again placed upon ordinary diet.

A properly applied dressing, such as described, will apparently cause the animal no discomfort, and it will wear for weeks without

adjustment of any kind; but it is best to remove it after the wound is well healed, say in ten days to two weeks, after which the animal is removed to the permanent quarters. Should swelling of the lower jaw occur, the dressing should be examined closely, and if it appears to be too tight the bandages are to be slackened. A too snugly fitting bandage may be the sole cause of the swelling, especially if it presses too strongly under the surface of the throat near the larynx.

Coagulation of Blood.

Since the question of clot formation is so intimately related to the question of blood-vessel surgery, a consideration of the mechanism of coagulation as it is looked upon by modern physiologists must form a basis of any interpretation of phenomena of this class observed in blood-vessel anastomosis and other similar conditions.

Until a few years ago, fibrin—the appearance of which in blood is considered the essential phenomenon of clotting—was held by many to result from the action, under favourable conditions, of fibrin ferment upon fibrinogen in the presence of soluble calcium salt, an insoluble calcium-protein compound (fibrin), formed under the influence of the ferment. This conception may be simply shown by the following diagrammatic equation:

Fibrinogen + calcium + fibrin ferment = Fibrin.

Later investigations indicate that the processes concerned may be further isolated and studied, and that the rôle of calcium is different from that which is accredited to it by the older views. The present view of many physiologists is as follows:

Fibrin is formed from fibrinogen under the influence of fibrin ferment, even in the absence of calcium. Fibrin ferment is formed from a substance termed "thrombogen," which is derived from blood-platelets. Since it is known that blood-platelets occur in the blood within the blood-vessels (Osler), and that blood shed in ordinary ways contains few, if any, blood-platelets, it seems clea that the belief that the blood-platelets rapidly break up under wha are recognized as favourable coagulative conditions—for exampl the contact of blood with foreign or rough surfaces. Thus a abundant supply of fibrin ferment forming substance is automat cally provided where needed—*i.e.*, at the point of hæmorrhage.

Under the influence of a substance termed "thrombokinase, thrombogen, in the presence of a solution of calcium salts, yiel fibrin ferment. The substance, thrombokinase, is not a tr

ferment, for it is itself used up in the reaction with thrombogen and calcium—that is, its action is quantitative. Such a substance is obtainable from most tissues of the body. The method usually employed is to finely grind the tissue to be tested and to extract the material thus obtained with water or diluted aqueous salt solution. In this way evidence has been obtained that different tissues exhibit evidences of differences in richness of the substance; but most tissues apparently contain a sufficient amount to insure coagulation of blood coming in contact with their surfaces after injury to them. Another source of thrombokinase is white blood-corpuscles; and perhaps blood-platelets themselves yielded a certain amount of the substance by their disintegration. It is stated that the white blood-cells in man do not suffer complete disintegrative changes when blood is shed. But it cannot be assumed that they do not liberate such substances under such conditions, and it is known that they are relatively rich in thrombokinase.

The reaction resulting in the formation of fibrin ferment may be represented diagrammatically as follows:

Thrombogen + calcium + thrombokinase = Fibrin ferment;

and the reaction resulting in the formation of fibrin thus:

Fibrinogen + fibrin ferment = Fibrin.

Howell states that thrombin probably does not act upon fibrinogen after the manner of an enzyme. Increasing amounts of thrombin give increasing amounts of fibrin, although in decreasing proportions. He further states that pro-thrombin may be converted into thrombin in solutions free from calcium salts.

In addition to the above outline, which, though brief and incomplete, presents the major current conceptions of the mechanisms of blood coagulation, a brief résumé of certain factors that are known to accelerate or to retard coagulative processes will be given in order to facilitate the presentation of the consideration of coagulation in relation to vascular suture.

It has been held for a very long time that if a segment of blood-vessel, such as an external jugular vein, be ligated at either end, and removed from the body, the blood contained therein will remain fluid almost indefinitely. If after a time the segment is opened and the blood permitted to come in contact either with an injured portion of the tissue—that is, a portion not covered with unruptured endothelium, or with any other foreign surface, even the air—coagulation will be induced. The explanation of these phenomena seems

to be that so long as the blood is in contact with intact vascular endothelial surfaces only, the fibrin ferment factors, thrombogen and thrombokinase, are but slowly liberated from the formed elements from which they are derived. So the clotting tendency is not so rapidly developed as when blood comes in contact with foreign surfaces.

The nature of the foreign surface is important in determining the rate with which blood will clot. For example, a raw tissue surface not only acts as a foreign surface in causing disintegrative changes in the organized elements that supply ferment factors, but itself contributes thrombokinase. Thus we have an illustration of an automatic protective mechanism devised by Nature for controlling hæmorrhage. Other foreign surfaces, inert in the sense of actually contributing a ferment factor, vary greatly in their property of hastening the coagulation process. In a measure this is due, apparently, to the ratio of actual surface to unit of blood. For a roughened surface is said to hasten coagulation more than a smooth one; but the nature of the substance presenting the surface appears to be a factor, as it is commonly stated that under otherwise similar conditions blood in contact with an oiled surface will clot more slowly than blood in contact with an unoiled surface.

Some of these facts have been made use of by surgeons almost from time immemorial. For example, a very old remedy for controlling hæmorrhage was to apply cobwebs, earth, or lint to the wound, and to-day the troublesome oozing from the diploë of the cranial walls is sometimes controlled by the application of some fibred material, such as cotton. And in transfusing blood oil-coated tubes are employed.

In operations upon blood-vessels it is obvious that conditions leading to the formation of occluding thrombi must be avoided if patency of the lumen is to be preserved. Therefore no manipulation of the vessel is practised that may jeopardize the result through injury of the intima, and it is for this reason that overstretching or handling with forceps, which might rupture or crush the intima, is avoided; and it is for the same reason that extreme care is necessary in applying the instruments by means of which temporary occlusion is produced; and it is for similar, though not identical reasons, that after temporary occlusion and section of the vessel the blood within its lumen is removed as rapidly and completely as possible —that is, clotting is avoided in order not only to prevent the occurrence of an excessive amount of fibrin ferment within the

vessel, but to avoid the possibility of fibrin being present within the vessel after the operation is completed. For it is known that intravascular clotting may be produced by the introduction of fibrin ferment in sufficient amount into the circulation; and that the presence of fibrin within a vessel is prone to lead to thrombus formation, for it not only acts as a foreign body, but it has the curious property of absorbing or otherwise attaching to itself a relatively large amount of fibrin ferment, though the latter, as before pointed out, is not considered as a structural constituent of fibrin. So it seems logical to remove the blood before much fibrin ferment is formed and before fibrin is laid down, for the reasons given and for the reason that fibrin is much more difficult to remove than the unclotted blood.

By thorough sponging of the cut surface and lumen of the divided vessels, not only is the blood effectively and safely removed, but juices from the cut tissues are also removed. Further, the application of a thin coating of oil serves the function of covering over, or in a way sealing up, the raw surface, thus tending to render it less able to subsequently favour fibrin formation; but in addition to this, oil thus applied not only facilitates the suturing by weakening the cohesive power of the vessel for the ligature, but protects the tissues from drying during their exposure to the air. This is an important consideration, and it becomes of graver magnitude when small vessels are operated upon. It should be remembered that oil itself is not wholly devoid of action on the tissues, and for that reason it should be used in moderation; but when properly used, as the algebraic sum of its action is benign, it should be dispensed with only after careful study. It is obvious that in very humid air the drying factor decreases in seriousness, and that the degree of drying during a short operation is proportionally less than during a longer one. So in this respect the optimum conditions are fulfilled when the operation is rapidly performed in a moisture-ladened atmosphere, and a minimum of oil used. I may say that under the first two conditions just mentioned my own inclinations would be to dispense with the oil entirely; but since successful results are achieved in slow operations, and when oil is abundantly used—that is, from the standpoint of securing a good functional result so far as the circulation is concerned—the operator entering this field should not dispense with the oil until he has satisfied himself that he has arrived at the point where he can practically control the result by his skill and speed.

The employment of salt solution upon cut edges of the tissues or inside the lumen of the vessel is not recommended, for it tends to contaminate the lumen of the vessel with tissue juice; it is not altogether without harmful action on tissues; and since excellent results are obtained by the method already described for freeing the vessel of blood, it unnecessarily complicates the technique and lengthens the time of the operation; besides, it tends to make the wound sloppy. So it is recommended that its use be restricted to the outer surface of the vessel, if its use seems necessary to prevent undue drying, and to its application to the other tissues exposed during the operation. Used for these purposes, it is best applied with a moistened, but not a dripping, sponge. Its further use is discussed in the division on technique; and the reason for the view that it is not without harmful action is stated in the division on the preservation of vitality of tissues (p. 115).

But to emphasize these points, it may be said that the best preservation of normal macroscopical and microscopical structure has been observed in the most rapid operations, and with the minimal use of oil and salt solution. And this must be so even if experimental proofs were lacking, for normality of structure depends upon normality of conditions, and exposure and manipulation of blood-vessels, and their treatment with oil and salt solution are abnormal conditions. And since this is not a consideration of the degree to which blood-vessels may be exposed to abnorm conditions without losing their normal structure and functions, b a consideration of measures devised for the purpose of permitti operations upon blood-vessels with the minimal alteration of norm conditions, discussion need not be further pursued.

Considering now, from the coagulation standpoint, the line of approximation of the divided edges of the vessel and the presence of the suture within the lumen, we are able to introduce some interesting observations that go a long way toward explaining the experimental findings—that is, the very excellent preservation of anatomical structure, including patency of the lumen.

If the ends of a divided blood-vessel be sutured together, and then a segment of the vessel bearing the anastomosis be immediately cut out and laid open longitudinally, which may be quickly done by means of a pair of small scissors, the condition of the intimal surface at the point operated upon can be studied. In a perfect operation a narrow transverse area is seen. It is limited on either side by the needle punctures which are themselves connected by the stitches

lying in grooves, which gives the band-like suture area a corrugated appearance. The thread appears to fill the needle holes, but its surface is exposed to the lumen of the vessel as it passes across from hole to hole. The junction of the intimal edges is to be seen as a transverse line, but little if any raw surface is exposed. In a way, the intimas present an appearance of being matted together. Of course, no knots are visible, as they are invariably tied on the external or adventitial surface of the vessel. On the whole, the anastomosis presents a smooth though somewhat corrugated or puckered appearance, from the intimal surface, which is marked across by the stitches which lie in shallow grooves, due to the pressing of the material into the yielding intimal tissue by traction upon the thread during the operation. The semi-circumference of the stitch material crossing the suture zone is entirely exposed to the lumen of the

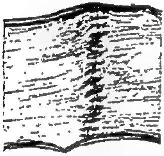


FIG. 36.—APPEARANCE OF INTIMAL SURFACE OF ANASTOMOSIS TWO HOURS AFTER UNION OF THE ENDS OF DIVIDED ARTERIES.

(Observed at distance of 1 yard.)

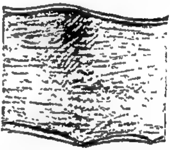


FIG. 37.—APPEARANCE OF INTIMAL SURFACE OF ANASTOMOSIS TWENTY DAYS AFTER UNION OF THE ENDS OF DIVIDED ARTERIES.

(Observed at distance of 1 yard).

vessel. With a lens it is usually possible to observe that continuity of the intimal surface is not so complete or perfect as the grosser examination indicates, as roughened intimal margins and even small gaps may be observed along the line of approximation of the intimas, and many or all of the needle holes, particularly on the sides away from the suture field, show raw areas and surfaces. The intimal surfaces of the stitches are seen to lie snugly in the grooves already described.

Now, it would seem that here we have favourable conditions for fibrin deposition, foreign surfaces—*i.e.*, surfaces capable of yielding thrombokinase—the raw tissues of the vessel walls exposed by gaps on the intima, and the stitches, rendered more or less inert so far as inducing the deposition of fibrin is concerned, by impregnation with oil, but certainly not without some action in this

lirection. It is true that the total area of such foreign surface does not seem very great relative to the whole intimal area, but it could not be predicted with certainty, from the facts thus far stated, whether or not an occluding thrombus would occur.

So after predicting the laying down of fibrin, at least on the raw surfaces, we turn to actual experimental findings for the answer to the main question—viz., preservation of patency of the vascular lumen. Considering the results of such examinations as described, only taking the segments at intervals of days and weeks after the operation, one finds that fibrinous deposits are laid down at least on the raw surfaces; but such deposits are relatively slight, and they very soon undergo resorptive changes and become protected with an intimal-like covering. The exposed threads are also quickly covered over with a similar coating, so that if examined with a lens the whole intimal surface appears to be continuous.*

Since this shows that the coagulant action of the blood has been exhibited, but, happily, in what may be considered only a benign way, we may conclude that the technique, though imperfect from the standpoint of avoiding the setting into activity of the coagulating property of the blood—is satisfactory from the practical standpoint—namely, the avoidance of the formation of an occluding thrombus, or a thrombus of size sufficient to embarrass the circulation through the anastomosis.

The somewhat peculiar nature of the fibrinous deposits in the interstices of the intima as described is more fully discussed in the division on results (p. 106).

So the occurrence of clotting in the manner described, and of the nature to be later considered, is regarded as a regular phenomenon of blood-vessel suture. It is looked upon as favouring the union of disrupted endothelial surfaces, for it acts not o[illegible] mechanically to close all minute openings through which bl[illegible] quickly results in causing the endothel[illegible] continuous, smooth, inert surface to [illegible] approximately the conditions of a norma[illegible]

The mechanism limiting the extent [illegible] is not clearly understood. But consid[illegible] produced by introduction of fibrin ferm[illegible]

* In a recent experiment eleven common carotid [illegible] veins of dogs were pierced transversely with from one [illegible] In some of the experiments the threads were oiled, [illegible] treated. Three weeks later the vessels were exam[illegible] be occluded.

is of interest—namely, the increase of antithrombin in the blood. It is commonly held that the liver is intimately concerned in this reaction. But be this as it may, it would seem that following blood-vessel suture, since a clotting-like action occurs, and it is possible that some fibrin ferment is formed that passes off into the blood-stream, a similar reaction may be induced. But the amount of ferment absorbed by the blood is probably very small, as the mass of the clot-like formation is slight, and fibrin is known to bind fibrin ferment in a curious manner, since it is not believed to be a chemical union. And therefore such reaction is probably too small to be detected by present experimental methods. So the formation of anticoagulant substances in this manner would seem to be a possible, though not very powerful, factor in limiting the clotting that occurs in the field of suture. Experimental observations confirm this view. For, in general, it may be stated that the magnitude of such thrombus formation apparently varies indirectly with the circulation—*i.e.*, the mass of blood per unit of intimal surface. This might be interpreted as being in favour of the anticoagulant view by supposing that, if a small increase in this property were induced by fibrin ferment as described, under conditions where the amount of blood passing over a unit area of internal surface was large, the anticoagulant action would be enhanced by the exposure of the injured surfaces or thrombus-covered surfaces to a greater quantity of blood—hence a greater quantity of anticoagulant substance would act upon a given area in a given time. But the character of the thrombi and a consideration of the mechanism of coagulation indicate that other factors are perhaps of greater importance. In brief, the thrombi are of the lamellar white type. Preceding their appearance, it is probable that the platelets and white corpuscles coming in contact with the raw surface, which, indeed, may actually attract them, or cause them to accumulate as by an agglutinative process, are so altered that the essential fibrin ferment pro-substances, thrombogen and thrombokinase, are liberated. And since calcium is present, fully formed ferment quickly appears at the site of injury. Direct coagulative processes then follow, and the raw surface is soon buried. That an adhesive mechanism exists is indicated by the gathering of the white blood-cells and platelets at the point, and by the clinging to the raw surface of the thrombus itself. But the nature of the process is not understood.

It seems reasonable to suppose that the degree of injury suffered

by a blood-cell through contact with a foreign surface will within limits vary with the period of exposure. And since it is through injury to the cells that the pro-fibrin ferment factors are liberated, the amounts of these will vary in the same way. If this is so, then it follows that a blood-platelet or white corpuscle would be more exposed to a given surface in inverse proportion to the speed with which they are carried; and that degree of injury, hence amount of pro-ferment factors liberated, will likewise vary with the circulation. Further, the number of blood-platelets or white corpuscles in proportion to the mass of blood passing through the vessel which come directly in contact with the wall varies indirectly with the diameter of the blood-stream, and therefore the tendency for coagulation per unit mass of blood will, from this standpoint, be greater in a small one.

But since the same sizes of needles and threads are used for vessels in the smaller class, which individually var[illegible] in size, not only are the needle punctures and stitch [illegible]portionately greater collectively in the smallest vess[illegible] vidually as well.

To sum up, we may conclude that a large number of [illegible] concern the question of coagulative processes, and th[illegible] such processes, many of which are little understood [illegible] considered singly. So how complicated the problem be[illegible] they are considered collectively, and a prognosis of th[illegible] specific intimal injury attempted!

To simplify the conception of the relations of the mor[illegible] factors concerned, the following standpoint is taken by [illegible] Thrombus formation after intimal injury, or the introd[illegible] foreign body into the lumen of a blood-vessel, as a sutur[illegible] directly as to (1) the ratio of injured or foreign surf[illegible] diameter of the lumen of the vessel; or (2) the degree of [illegible] pocket formation at the abnormal point; (3) the coagu[illegible] the blood. And it will vary indirectly as (1) the diam[illegible] vessel; or (2) the amount of blood passing the point in a gi[illegible] and (3) the velocity of the blood—*i.e.*, as the ratio of un[illegible] blood to endothelial area.

Exact values of these factors or methods of determinin[illegible] most cases are wanting, so it is impossible to express by [illegible] formula the ratios existing when thrombus formation [illegible] beyond the desirable degree. But perhaps it is not wholly [illegible] to desire such a state of knowledge.

Neither general nor local specific anticoagulant agents, such as leech extract (hirudin), have been employed. For successful results are easily achieved as described, and whether such restraint of coagulation would be on the whole desirable is doubtful. A certain amount of thrombus formation is highly desirable for the temporary repair of the blood-vessel, so no leakage will occur; and it would be undesirable to diminish general coagulability on account of the danger of the difficulty that would ensue in securing a "dry" wound.

REFERENCES.

BARTLETT: *Centralblatt f. Chir.*, *1905*, No. 15.

CARREL AND GUTHRIE: S. G. O., 1906, ii. 266.

GUTHRIE: Wash. Univ. Bul., June, 1907; Am. Jr. of Phy., 1907, xix. 482; Jr. of the Am. Med. Assoc., 1908, li. 1658; Wash. Univ. Bul., 1908, vii. 40; Interstate Med. Journ., 1908, xv. No. 6.

GUTHRIE, C. C., AND F. V.: Jr. of the Am. Med. Assoc., 1910, liv. 349.

HOWELL: Am. Jr. of Phy., 1910, xxvi. 453.

OSLER: Stewart's Manual of Physiology, 1910; sixth ed.

CHAPTER III

OPERATIONS UPON BLOOD-VESSELS

In the section devoted to a detailed description of operative technique, direct end-to-end anastomosis of two ends of transversely divided vessels was chosen as being a representative operation. And much of the procedure described is applicable to any operation involving the suturing together of the walls on any blood-vessel in which the lumen is opened. In certain operations, however, some of the manipulations are not practised, and certain other procedures are carried out. So the common operations will be described in order that essential differences in technical procedures may be considered in relation to their actual application, and also for the purpose of indicating by concrete examples the extent to which blood-vessels may be operated upon with good functional results as regards institution, restitution and preservation of free circulatory channels.

The simplest class of operations deal with the repair of wounds in the walls of blood-vessels, either arteries or veins. In general this is best accomplished by freely exposing and temporarily occluding the vessel on either side of the point of injury, and stitching the edges of the wall together by means of a continuous suture, in much the same manner as described for the closing of leaks in an imperfect end-to-end anastomosis (p. 49). If only a few stitches are required, and if they can be quickly placed, the blood within the segment of vessel temporarily shut off from the circulation need not be considered; but if several minutes must elapse between the shutting off and the restoration of the circulation, the excess of blood must be removed, as even moderate coagulation within the vessel, for reasons already stated (p. 56), very seriously jeopardizes the result aimed at. The blood may be removed sufficiently well by the stripping and sponging technique—that is, the vessel is compressed on both sides of the injury between the balls of the thumbs and

index-fingers placed close to the temporary hæmostatic clamps, and by gentle, and two or three times repeated, stripping movements carried to the injury, the blood is pressed out of the vessel through the opening resulting from the injury and absorbed by a dry cotton-gauze sponge, held tightly against it. Or if for any reason this is not feasible, one of the clamps employed for temporary shutting out of the circulation may be released sufficiently at minute intervals to permit sufficient blood to enter to displace the stationary blood contained in the lumen, thus, by a process of displacement and refilling, to permit no blood to remain in the segment for coagulation to take place. But the method of removing the blood is much the more desirable. The edges of the wound should be trimmed slightly if too ragged. This may be conveniently done by grasping both edges of the lips of the wound with the tips of the blades of a pair of round-nosed dissecting forceps, and while stretching the walls outward by gently applied traction on the forceps to snip off the edges with a single clip of a pair of small, keen scissors held longitudinal and parallel with the surface of the vessel. Whenever possible, and when the resulting stenosis will not be too great, scissors are used, not only because the amount of tissue removed can be very accurately gauged, but because both sides of the wound will be counterparts—a very important feature in all plastic work. Scissors with curved blades are excellent for this purpose. The reason for making a longitudinal cut with the scissors is that less tension will be exerted on the suture after the wound is closed. Of course, some constriction of the lumen is inevitable, but by exercising care to save all of the sound tissue possible, the chances are that in simple injuries this factor will not be appreciable, as the lumen of a blood-vessel may be considerably narrowed permanently without imperilling the function of the tissues supplied by the vessel through circulatory failure (see p. 142).

After the margins of the wound have been prepared—and too much emphasis cannot be laid upon the desirability of avoiding removal of more tissue than is necessary to give regular edges for suturing—the lips are brought together by pressing the vessel between the ball of the left thumb and forefinger, so that it is flattened and the raw edges of the wall appear on one edge, and are stitched together by a continuous suture. Beginning at one end, the first stitch is placed about 1 millimetre back from the end of the wound; it extends through both walls, but barely penetrates

the intima. It is drawn well through, and the two ends doubly knotted firmly against the external surface of the vessel. The remainder of the stitches are similarly placed along the margins of the lips of the wound, penetrating the coats of the vessel about $\frac{1}{2}$ millimetre from the raw edges of the lips, and being placed at intervals of about the same distance. Each, or every other, stitch

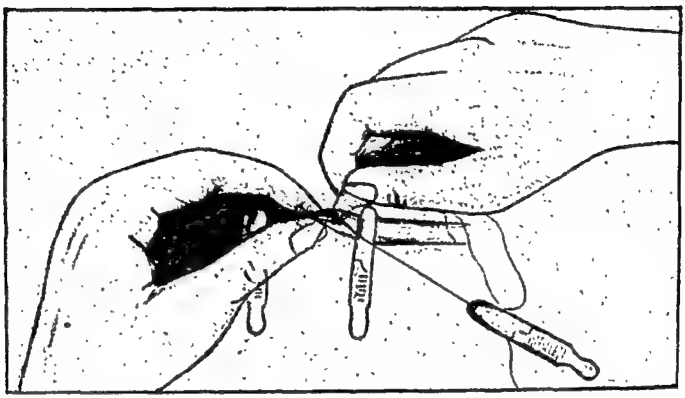


FIG. 38.—REPAIR OF LONGITUDINAL SLIT IN BLOOD-VESSEL WITH FINE CAMBRIC OR LACE NEEDLE AND THREAD, SHOWING POSITION OF HANDS.

is gently but firmly drawn until all slack is taken up and the endothelial margins are firmly and continuously approximated. When the extremity of the wound is reached, a last stitch, corresponding to the first, is placed, and the end of the suture tied in precisely the same manner as in sewing a skin wound (p. 51). In fact, the technique for thus sewing together the edges of a wound in a blood-vessel differs only from that described for the skin in the nature and

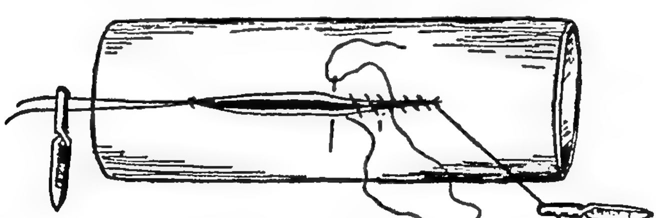


FIG. 39.—REPAIR OF LONGITUDINAL INJURY IN A BLOOD-VESSEL BY MEANS OF CONTINUOUS THROUGH-AND-THROUGH SUTURE, SHOWING MANNER OF STITCHING.

delicacy of the needle and suture material. The operation is concluded by snipping off the ends of the suture close to the vessel and restoring the circulation by removing the temporary hæmostatic clamps, and observing and treating the line of suture as in the case of end-to-end anastomosis.

In the case of small, more or less circular openings, the few

stitches necessary may be placed without tying the first one, and the ends tied above the stitches collectively. And with such small wounds it may be possible to pick up the vessel on the ball of the index-finger, and to close it without other manipulation—*e.g.*, as described for repairing a fault in an imperfect end-to-end anasto-

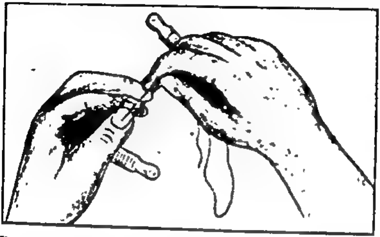


FIG. 40.—REPAIR OF TRANSVERSE SLIT IN BLOOD-VESSEL WITH FINE CAMBRIC OR LACE NEEDLE AND THREAD, SHOWING METHOD OF HOLDING VESSEL ON FINGER.

mosis (p. 49). Thus the damage may be repaired without producing temporary hæmostasis by means of clamps.

Quite recently an ingenious clamp for temporarily isolating and shutting off the blood from an injury in a vessel, but which permits the circulation to continue through the restricted lumen, has been devised and described by Professor Stewart. As shown in the figures (p. 68), the essential features of the clamp are as follows:

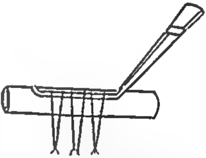


FIG. 41.—JOANI'S CLAMP APPLIED FOR SHUTTING OFF THE CIRCULATION TO A PORTION OF THE WALL OF A BLOOD-VESSEL.

The long, narrow grip of the jaws on the longitudinal direction. The grip is narrow in order that as little as possible of the lumen may be encroached on. The extension of the grip at each end, at right angles to the length of the vessel, is necessary to complete the occlusion of the isolated segment. The length of the rectangular portions should be proportioned to the diameter of the vessel worked with. If too long, they project too far beyond the vessel and thus make the field of operation less accessible for some purposes. The size of the hollow beyond the gripping edges must be great enough

to accommodate the non-occluded part of the vessel without occluding it.

As pointed out by Professor Stewart, such clamps might be employed to arrest hæmorrhage from a wound in a large vessel, which could not be clamped completely without detriment, and during the suturing of the wound; possibly in the treatment of sacculated aneurism in some situations; in performing lateral anastomosis of blood-vessels in cases where it is undesirable to completely occlude one or both of the vessels for the time required in the operation; in performing lateral implantation of one vessel on to another which must not be totally occluded; in inserting a cannula laterally into a vessel without stopping the circulation, when there is no convenient branch of the vessel which might be used, or when it is disadvantageous to occlude such a branch; in narrowing experimentally the lumen of a vessel without temporarily occluding it, especially when a diminution of the lumen by a definite amount is desirable.

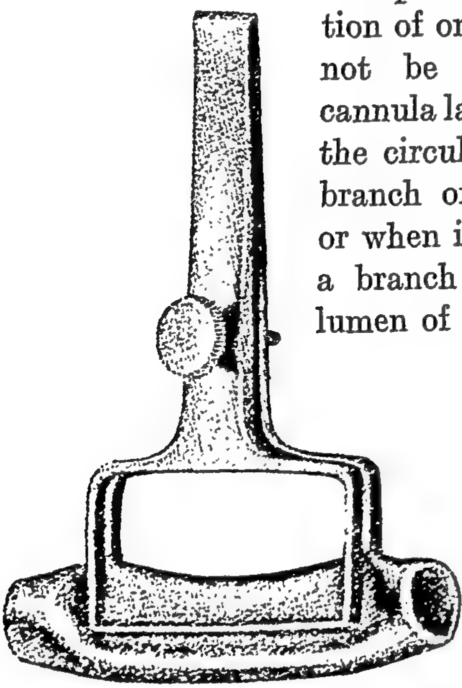


Fig. 42.—Clamp to be applied to the Wounded Side of the Vessel only. (Stewart.)

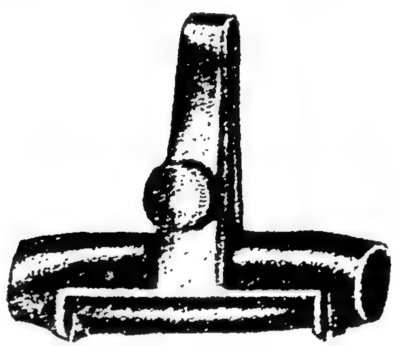


Fig. 43.—Form of Clamp with a Screw for graduating the Pressure. (Stewart.)

The complete temporary shutting off of the circulation in certain tissues is open to very grave objection, for it is known that certain tissues are exceedingly susceptible to temporary anæmia, and irreparable injury may thus be produced. This is true especially of the brain. But a relatively small amount of blood may suffice to maintain even the brain in such a condition that good return of function is possible with restored circulation after considerable periods of profound though incomplete anæmia (Hill). But, fortunately, owing to collateral circulatory channels, even such

vessels as the descending aorta may for a time be completely occluded without serious permanent derangement of function of the tissues thus temporarily deprived of much of their blood-supply; indeed, surprisingly slight derangement of function, after comparatively rapid and complete occlusion of the abdominal aorta just posterior to the renal arteries, has been observed by the writer. The animal was a cat (p. 244, Cat 32). The aorta was pletely occluded both above and below the renal arteries for twenty-five minutes. Owing to bungling manipulation, particularly of a trocar thrust into the aorta just posterior to the renal vessels, the vessel was very severely injured. For a period of several days following the operation some paralytic symptoms were noted in the hind-quarters, but these disappeared completely. Twenty days after the operation the animal was chloroformed, and at post-mortem examination the aorta was found to be completely occluded by an organized thrombus, situated just posterior to the renal vessels. Now, all the facts in this case indicate that the aorta became completely occluded within a comparatively brief period after the operation. Yet the condition gave rise to only moderate and temporary derangement of function. One striking feature of the results, though not bearing directly on the major problem, may be mentioned—viz., the result of injury to the aortic intima. In two cases only have we observed occluding thrombi in the aorta, and in both cases the result was due to gross fault in technical procedure, by which not only the intima, but the outer walls of the aorta, were crushed and otherwise maltreated. In one case the thrombus extended for some distance both above and below the origin of the renal arteries, and the cat died during the first day.

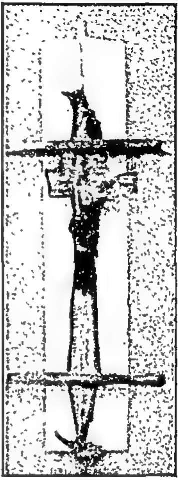


FIG. 44.—AORTA OF CAT 32, SHOWING OCCLUSION BY THROMBUS JUST POSTERIOR TO RENAL ARTERIES.

Kidneys perfused with salt solution, January 26. Cat killed February 15.

(*Archives of Internal Medicine*, 1910, v. 232.)

Similar observations on the effects of aortic occlusion have been

made, and the literature, which has been reviewed by Halstead, who himself has made numerous experiments and observations, is fairly voluminous (p. 143). In view of this it is well to be careful in drawing conclusions as to patency of lumen after operations upon blood-vessels from lack of, or disappearance of, symptoms attributable to occlusion of the vessel. A case in point is that of Braun, who resected a segment of the abdominal aorta of a child and sutured the ends of the vessel together. Twelve days later the child was in good condition, and the inference has been drawn that the operation upon the aorta itself was successful; but though this might easily be true, it by no means follows from the observation. For occluding aortic thrombosis might occur; the clinical observations would be the same as those reported.

It is safe to say that when patency of the lumen of a blood-vessel can be preserved, even though the lumen is greatly decreased in size, it is better to repair it by suturing than to ligate it. For even though the circulation may for a time be inadequate for the normal nutrition of the tissues supplied, they may be tided over the period necessary for an adequate circulation to become established through collateral channels, and the tissue may then be able to recover and assume its full duties.

In the event that so much of the vascular wall is missing or has to be removed that preservation of patency of the lumen becomes a matter of grave doubt, then one has the choice of four things —viz., ligating on either side of the injury; restoring the vessel wall by means of a patch; dividing the vessel transversely on either side of the wound and directly anastomosing the ends; or, after removing the injured segment, to interpose a segment of another blood-vessel or similar tubular segment and restoring the continuity of the vessel by anastomosing its ends to the ends of the vessel.

Ligations may be safely practised upon vessels of secondary size and importance, as, for example, the ulnar artery. Here the parts supplied have very abundant anastomotic connections, so ligation of the artery mentioned will produce little alteration of the blood-supply, as the anastomotic channels will quickly become adjusted to the increased demand made upon them. As an example of an intermediate type of vessel, the brachial artery may be mentioned. Ligation here is much more serious, and though care be taken with such vessels to preserve to the greatest extent possible all branches which from their position, size, and distribution are the most important in the establishment of an adequate anasto-

motic circulation, less perfect results can be predicted with certainty. Of the more extreme type, the renal artery is a good example, for when, as in the majority of instances, the kidney is supplied with but a single main artery, shutting off of the circulation through the vessel is surely followed by profound disturbance of function of the organ; and notwithstanding that the kidney receives some blood through other vessels (particularly by way of the ureter) this is so meagre that the organ will undergo extensive degenerative changes after the renal artery is tied. But it is well to bear in mind that not infrequently the kidney is supplied by more than one renal artery (see p. 200). In such a case the tying of one trunk would be a different matter.

Another example that is of particular interest, in view of the somewhat divergent views expressed as to the results after ligation, is the common carotid arteries. It is commonly held by surgeons that in man ligation of even a single common carotid artery is a grave procedure owing to the danger of serious derangement of the blood-supply of the brain. An examination of the literature on this subject does not bear this out from anatomical and experimental physiological standpoints; for, though a relative difference in the blood-carrying capacity of the cerebral arteries of different animals and the relation of blood-supply to cerebral activity is admitted, yet, since what may be termed the secondary or reserve or anastomotic circulatory channels are at least not markedly restricted in the morphological sense, it is rather surprising to the experimentalist that such a difference exists in man as compared to lower animals, for both common carotid arteries may be permanently ligated at the same time in many of the lower animals, with the production of scarcely any objective symptoms, or none at all. The brain is exceedingly susceptible to alterations of its blood-supply, yet the writer has completely occluded, by direct compression, both common carotid arteries in man for a period sufficient for the removal of the whole of the lower jaw, the object of the arterial compression being the control of hæmorrhage, which was very successfully accomplished, and yet the minutest observation failed to reveal any evidence of inadequacy of cerebral circulation. The patient, though unconscious from ether, was not in a deep stage of narcosis, and such eye reflexes as were present were not visibly diminished by carotid occlusion, nor was there any marked change in respiratory rate, and no post-operative symptoms attributable to the compression of the carotids were observed

through the brief period over which observations extended (*cf.* p. 149). Notwithstanding this, it is known that simultaneous compression of both common carotid and both vertebral arteries in similarly anæsthetized cats or dogs is quickly followed by marked evidences of inadequate cerebral circulation—viz., disappearance of ocula reflexes, dilation of the pupils, and cessation of respiratory move ments; while carotid compression alone gives slight or no evidenc of such a condition (p. 315). The writer does not stand alone in th view that the carotid arteries may with safety be compressed, Professor Hill, after much experimentation and study, stated t in his belief, if gradually occluded at intervals, both carotids both vertebral arteries might be safely tied in man. He menti a case of practically complete occlusion of these four arteries in m by a pathological process, without ill effects. Hill emphasizes t importance of gradual compression of the arteries to avoid unfavo able results.

But in order to avoid the possibility of being misunderstood, will state that, though present experimental evidence does n speak against either temporary or permanent occlusion of tl common carotid arteries, yet, owing to contradictory clinic observation on man after permanent occlusion of even a sing common carotid artery, the question must be considered as n settled, and therefore all considerations must be carefully weighe before practising such occlusions on man. As a precautionar measure it is suggested that, when ligation is definitely decide upon, it would be well to temporarily compress the artery for period, and to very carefully observe the results upon the ey reflexes, discharge of the respiratory and motor centres, or othe manifestation, before permanently fixing the ligature. For from what is known it would seem that if no objective symptoms were produced by the temporary occlusion, the occurrence of symptoms after permanent ligation would be less probable than if symptoms were observed in the first instance (see p. 150).

Restitution of the vascular channel by laying a patch in the opening made by injury is feasible; but excepting for experimental purposes, it will probably be rarely employed; for, in addition to being a more complicated and difficult method, it is employed only in such cases as may not be successfully handled by simple suture of the edges of the wound directly in so far as restitution of patency of the lumen is concerned. So the indication for its employment narrows to a consideration of those cases where constriction of the lumen

occurs, which necessarily follows repair by simple suture when portions of the vascular wall are actually missing or have to be removed, in which the effect of narrowing of the lumen upon the subsequent functioning of the tissues affected is serious. For example, in the case of an injured vessel which supplies a tissue whose resistance to poor circulatory conditions is weak, and is poorly supplied with anastomotic blood-channels, and therefore may be seriously affected by constriction of the artery, it would probably be better to patch the artery in order to retain a lumen of adequate size. But since the danger of serious thrombus formation will be greater in patching than in simple closure of the wound, owing to the relative increase of foreign surfaces in proportion to the diameter of the vessel, other considerations must enter into the final decision, as the removal of a partial or complete segment of the artery bearing the injury and direct suture of the walls, or complete removal of a segment and the interposition and suture of a suitable tubular segment between the

FIG. 45.—SHOWING SEGMENT OF VEIN INTERPOSED BETWEEN AND SUTURED TO THE ENDS OF A DIVIDED ARTERY.

ends. All factors must be as carefully considered as possible in each individual case, in order that the operation offering the best chance of success may be selected.

In case the injury is so extensive as to necessitate the removal of a complete segment of a vessel, vascular continuity may be restored by direct anastomosis of the ends, which can be accomplished by following the technique already described. But if much tension is necessary to bring the ends together, either through the removal of a long segment or the retraction of the ends of the vessel after division, it is best to employ a suitable tubular segment to restore the circulatory channel. An ideal segment for this purpose would be one from the same artery, but as this is not practicable, then such a segment from a similar animal or from a different species of animal, or a venous segment from the same animal, may be employed. The segment selected should be of about the same size as the artery, and it should be cut of a length

usual way, the circulation restored, and the operation finished as in the case of a simple anastomosis. Any branch on the segment not previously ligated is tied close to its mouth, using a small silk ligature for the purpose. By this method large vascular tracts may be removed, and satisfactory re-establishment of the channel accomplished.

The operation of direct end-to-end anastomosis of arteries has been sufficiently described for vessels of similar size (p. 44). In the case of thus uniting the ends of two vessels varying considerably in size it is necessary in sewing the edges together to uniformly take longer stitches in the edge of the larger vessel in order that the excess of wall may be evenly distributed around the entire circumference of the line of suture. When this is properly done, vessels of very unequal size may be very satisfactorily united. (Figs. 46 and 47.)

What has been said of arteries is true also of veins. The technique is the same for both.

Also it is a very simple matter to successfully unite the ends of arteries and veins together. Since comparable arteries and veins are most convenient as regards proximity, operations thus far have been performed most frequently upon such vessels, as the common carotid artery and the external jugular vein; and as the vein is usually of the greater diameter, the same precautions are observed in making the union to avoid "puckering," as described for arteries of unequal size. By such operations the character and the direction of the circulation in veins and arteries may be changed almost at will. For example, if the central end of a common carotid artery be anastomosed to the peripheral end of an external jugular vein, the circulation in the latter becomes arterial in character, and the direction of flow is reversed. Or if the central end of a common carotid artery be connected with the central end of an external jugular vein, the character of flow in the latter becomes arterial. Likewise, if the femoral artery and vein be divided, and the ends crossed and united (central ends to peripheral ends), the venous channels peripheral to the line of operation carry arterial blood to the capillaries—*i.e.*, in the direction reverse of the normal—while

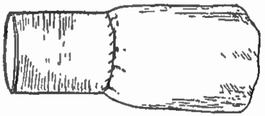


FIG. 48.—END-TO-END UNION OF AN ARTERY AND VEIN, SHOWING CONSTRICTION OF THE END OF THE VEIN TO CONFORM TO THE ARTERY.

the peripheral arterial channels return the blood back from the capillaries—that is, the arteries convey venous blood, and the direction of flow is the reverse of the normal (see p. 161).

But a vein may be with ease successfully united end-to-end with an artery much larger than itself. Thus the peripheral end of an inferior thyroid vein may be united with the central end of a common cartoid artery. Care is taken to uniformly take longer stitches in the edge of the artery in order to obtain a smooth, regular union. The results of all such operations, not only upon the vessels themselves (p. 83), but the results upon the tissues affected (p. 174) will be considered more fully in separate divisions.

Thus far only suturing of vascular injuries, including patching and end-to-end anastomoses, and interposition of tubular segments and suture of their ends to the ends of divided blood-vessels, have been considered. But other operations, consisting of anastomoses between the ends of vessels and lateral openings in the walls of vessels, for convenience termed "termino-lateral" or "end-to-side anastomosis," and anastomoses by lateral openings, termed "lateral" or "side-to-side anastomosis," are of interest and importance.

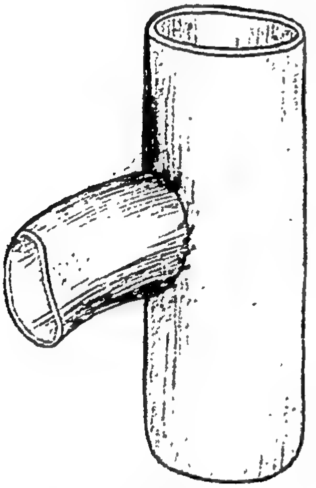


FIG. 49.—END-TO-SIDE ANASTOMOSIS.

A termino-lateral or end-to-side anastomosis is performed by dividing a vessel, and preparing one end as described for an end-to-end anastomosis. The vessel into which the end is to be implanted is isolated, and a segment temporarily cut off from the circulation by suitable clamps. A circular opening, slightly larger than the lumen of the end of the vessel already prepared, is then made by removing a disc from the wall. This is done by firmly grasping the tissues of the wall at a point corresponding to the centre of the proposed opening, and removing the disc with keen scissors having curved blades. The blood is then pressed out of the segment, and removed with a sponge, as described for the preparation of a ragged injury in a vessel wall for suture (p. 65).

Next a fixing suture is passed from without inward through the edge of the wall, as in end-to-end suture, and a point on the edge of the wall of the end of the other vessel is pierced from within outward, and the ligature loosely tied and held while the second

fixing suture is placed. The first suture is the undermost one, considering the position in which the vessels will lie after the operation, and care is exercised to avoid distortion or unnecessary bending of the artery. The second suture is similarly placed one-third of the distance around the circumference of the lateral opening and of the margin of the end of the vessel. The two ligatures are then tied, and the last fixing suture placed and tied at the apex of the isosceles triangle, whose base is formed by the first and second stitches. Or four fixing sutures placed at equidistant points may be used. The cut edges of the vessels between the fixing ligatures are then continuously stitched together in the same way as in end-to-end anastomosis, and the operation completed by cutting off the ligatures, restoring the circulation, and closing the wound. This operation is especially indicated when an increased blood-supply for a part is desired, and at the same time it is undesirable to sacrifice the circulation through the vessel from which the supply is to be drawn, for example, in the arterialization and reversal of the circulation in the inferior thyroid vein by implanting its peripheral end into one of the common carotid arteries.

FIG. 50.—SHOWING END-TO-SIDE METHOD OF UNITING BLOOD-VESSELS, A PATCH SURROUNDING THE MOUTH OF THE SMALL VESSEL BEING REMOVED AND IMPLANTED.

If the branch thus added to a vascular trunk is of such small calibre as to render the operation too difficult or the result doubtful, a circular disc of suitable size, bearing the orifice of the vessel in its centre, may be removed, and set into a suitable opening made on the trunk of a vessel for its reception, the technique being a combination of that described for the repair of a vascular injury by inserting a patch and for end-to-end or termino-lateral anastomosis. This operation is valuable, especially in engrafting masses of tissues or organs whose blood-supply is carried through vessels too small to handle in the end-to-end fashion, as an ovary. But this will again be mentioned in the section on transplantations (p. 200).

Lateral or side-to-side anastomoses are the oldest abnormal, direct, anastomotic connections between vascular trunks observed, being occasionally produced by the rupture of an aneurism into a vein, or through acute or traumatic injury of blood-vessels, as in stab-wounds, or wounds made in lancing vessels for the purpose of bleeding. The essential mechanism appears to be simultaneous opening of an artery and vein, with passage of the arterial blood

into the vein. Thus some of the arterial blood is "short circuited" back to the heart—that is, it returns to the heart without traversing the capillaries. The very fact that such permanent communicating channels have been observed under such conditions speaks m strongly for successful blood-vessel anastomoses and the ease wi which they may be performed. For under such circumstances tl conditions must be favourable for coagulation, yet in some instance at least permanently patent anastomotic openings result.

When examined more closely, the most powerful factors probably concerned in leading to the result—that is, the factors preventing the laying down of an occluding thrombus—substantiate the views of the writer as to the factors to be considered as preventing this undesirable result in deliberately planned and executed vascular anastomoses—namely, the velocity of blood flowing over the foreign surface, or the ratic of unit mass of blood per unit area of foreign surface (per unit of time).

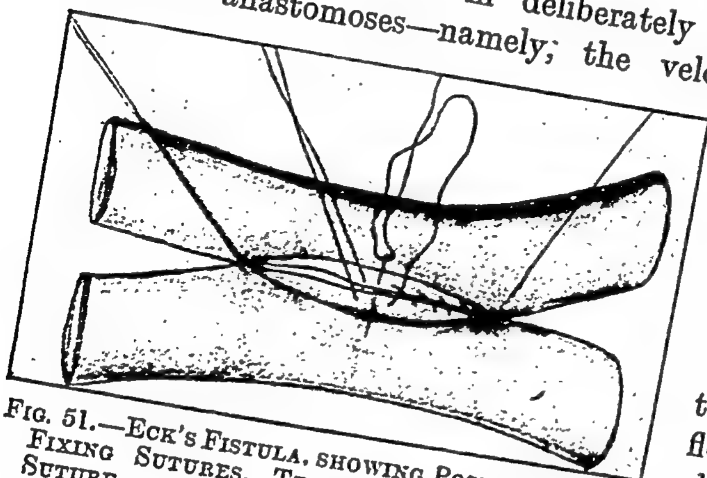


FIG. 51.—ECK'S FISTULA, SHOWING POSITION OF END-FIXING SUTURES, TEMPORARY MIDDLE FIXING SUTURE, AND METHOD OF SEWING FROM INTIMAL SURFACE.
Stitching should cross intimal surface transversely.

For in such cases the arterial blood flows through a short channel from an area of high arterial to area of low veno pressure. So th speed, and therefor the volume of blood crossing the foreign surfaces, must be relatively great. And in further substantiation of this view is the conclusion, from results of operative anastomoses, that the more exactly these conditions are imitated, the more certain a permanently successful result. As instances, arterio-venous anastomoses—*e.g.*, central end of a common carotid artery to the peripheral end of an external jugular vein, or lateral anastomosis of the portal vein to the inferior vena cava (Eck's fistula), with ligation of the former where it enters the liver, may be mentioned.

The technique of making a side-to-side anastomosis consists largely in the application of the methods already described, to the morphological conditions of the operation. Both vessels are prepared, and openings made in them, as in the case of the vessel used

as a trunk in end-to-side anastomoses. The openings are made of approximately equal size, and of the same shape, so that when the margins of the surrounding walls are brought together they fit evenly. The openings in the vessels should be in width about one-third the diameter, and in length about one and one-half times the diameter of the vessel, if the entire circulation of one vessel is to be diverted through the anastomosis, as in Eck's fistula, with ligation of the portal vein. As in all similar anastomoses, the posterior fixing suture is placed first. But it is placed from the intimal surface, and is not tied, being later removed. Next, a similar suture is placed on either side at points distant one-fourth of the circumference of the openings. The end sutures are placed in a special way. Directing the needle from without inward, it is thrust through the margin of the wall of one vessel at a point on an imaginary line drawn longitudinally through the centre of the lateral opening. It is then pulled through, and, with the point directed from within outward, it is thrust through the wall of the other vessel at the corresponding point. This leaves both ends of the suture outside of the vessels in the V at one end of the X formed by the trunks of the vessels. The suture is then tied, which places the knot in the crotch formed by the vessels. Beginning at one of the sutures last placed, which may be termed "end sutures," and holding the edges of the approximated walls in favourable position for suturing by traction on the first-placed suture, which is termed the "posterior," the edges of the vessel are sewn together by the usual continuous suture, the chief difference being that the outer or adventitial surfaces of the vessel margins are together, and not the intimal, as has been the case in previously described operations. And the points of entrance and exit of the needle are on the intimal surfaces. When the posterior ligature is reached, one of its ends that has been used for traction is severed near the tissue, and the remainder withdrawn. The ends of the other end-fixing suture previously placed, but not yet employed, are then used for traction

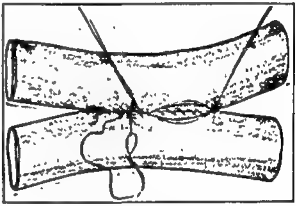


FIG. 52.—ECK'S FISTULA, SHOWING OPERATION NEARING COMPLETION.

upon the edges of the wall to be sutured, between the point wh it is placed and the posterior-fixing suture, and the laying of t continuous suture continued until the end-fixing suture is reache The continuous suture is then tied with this suture, the knot bein placed on the outer surface of the vascular wall. It should b noted that the continuous suture was not tied with the posterior suture. The reason for this is that it is unnecessary, and only serves to complicate and lengthen the operation. At this stage the edges sutured together appear rather rough, as they project inward and cause an abrupt longitudinal ridge on the lumenal aspect of the vessels. But the ridge formed by the edges of the vessels will largely or completely disappear owing to the pressing out of the walls and tension upon the line of suture—that is, by a kind of a leaf-hinge action, the edges will be moved outward, and the intima margins approximated.

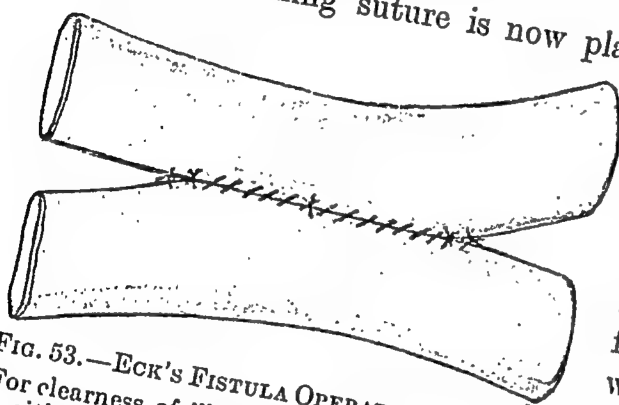


FIG. 53.—ECK'S FISTULA OPERATION COMPLETE. For clearness of illustration the stay sutures at either end of the anastomosis are not drawn tight.

A fourth fixing suture is now placed in the anterior margins of the walls in the usual manner, passing the needle from without midway between the end ligatures, and tied. The continuous suturing is then continued from the end ligatur where it was last tied t the fixing suture last placed, and tied with the loose ends. The remaining interval of free edges is then sutured, and the continuous suture tied with the end left at the original point of beginning. The ends of all ligatures are now clipped off within 1 or 2 millimetres of the vessels, the circulation restored, and the operation completed in the usual way. If much traction is likely to be exerted against the line of suture, it is well to place a staying suture in each crotch at either end of the suture line just distal to the primary end-fixing sutures, as these are the points of greatest strain. This is done by thrusting a needle, bearing a suture somewhat coarser than that used in suturing the edges of the vessels together, or the needle may carry an ordinary suture doubled, downward so as to take a firm stitch in the tissues of the wall of the vessel on one side of the crotch. The stitch need not penetrate the

intimal surface, but this is somewhat difficult to gauge, and no harm will result if it does penetrate the intima for a short distance if the suture used is not too coarse. The needle is then drawn through, and directing the point upward a similar stitch is taken in the wall of the opposite vessel, and the ends of the suture firmly and securely tied, and cut off.

Lateral anastomoses may be made between a ligated and divided vessel and the trunk of another vessel, or between two ligated and divided vessels, the lateral opening in the ligated vessels being made near the end in order to avoid an excess of "blind end" after the operation is completed. By means of the ligatures on the vessels, the ends may be fixed to surrounding tissues in such a way that excessive traction upon the anastomosis will be prevented. By using an ordinary surgical needle, into which the ligature is threaded, the operation of anchoring the end of the vessel is facilitated,

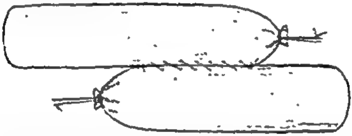


Fig. 54.—Termino-Lateral Anastomosis of Blood-Vessels.

The ligatures on the ends of the vessels are of service in preventing undue retraction and strain upon the anastomosis, the ligatures being fixed to neighbouring tissues (see Fig. 58).

as no time is lost in firmly and securely attaching the ligature to a suitable point of the surrounding tissues by means of a stitch.

Another anastomotic operation, which is of particular interest in connection with tissue transplantations and will be considered in the division on that subject (p. 201), consists in removing a segment of a vessel bearing the mouths of one or more branching vessels, and engrafting the segment by anastomosing the ends with those of a divided blood-vessel in the manner already described.

These are the most important operations of this character h practised upon blood-vessels, and it is left to the reader to of the merits or demerits of each from the evidence these pages. But the opinion of the writer is that it is to the various operations themselves to deal more one than with another, for no doubt the apparent cc the technique would tend to at least prejudice the

against some operations than others, while as a matter of experience some of the more complex appearing operations, as judged from the descriptions, are more successfully executed than certain of the more simple appearing ones. For example, an Eck's fistula is quickly and easily made. Even with methods much cruder in the sense that they leave more foreign surface exposed in the lumen of the operation than is the case with the method here described, the operation has been successfully performed many times in the last decade, and not infrequently by men of no considerable surgical experience. And the reason for this is clear when the occurrence of pathological or traumatic arterio-venous fistulas, in which class Eck's fistula in large measure belongs, although it is between veins, is considered (p. 77). Yet, as judged by the writer's description, the operation is among the more complex ones. So in forecasting a result many factors must be considered.

But all the operations described are perfectly successful as regards permanency of patency of lumenal openings and channels when properly executed and the conditions described fulfilled. So it may be concluded that not only are a large number of anastomotic operations on blood-vessels feasible, but the results as indicated by the circulatory function are satisfactory.

REFERENCES.

Braun: Archiv für Klin. Chir., lxxxvi. 707. *Cf.* Binnie, Surgery, 1910, ii. 13.

Carrel: Jr. of Exp. Med., 1907, ix. 226.

Carrel and Guthrie: S. G. and O., 1906, ii. 266; C. R. de la S. de B., 1906, lxi. 276; *ibid.*, 1906, lx. 1104.

Guthrie, C. C.: Jr. of the Am. Med. Assoc., 1908, li. 1658; Interstate Med. Journ., 1908, xv., No. 6; Archives of Internal Med., 1910, v. 232; Am. Jr. of Phy., 1907, xix. 482; Science, N.S., 1908, xxvii. 473; Jr. of the Am. Med. Assoc., 1908, l. 1035; Heart, 1910, ii. 115.

Guthrie, G. J.: On Arteries, 1830.

Halsted: Jr. of Exp. Med., 1909, xi. 373.

Hill: Cerebral Circulation, London, 1896.

Stewart: Jr. of the Am. Med. Assoc., 1910, lv. 647.

Watts: J. H. H. Bul., 1907, xviii. 153.

CHAPTER IV

MORPHOLOGICAL RESULTS

It is evident that many different combinations of blood-vessels are possible, ranging from simple suture of the ends of a divided arterial or venous trunk to the engrafting of a segment of vein between the ends of a divided artery, with reversal of the direction of the circulation in the venous segment. But in this place only such combinations as have yielded results that contribute definite knowledge of the structural character of blood-vessels after such operations will be described.

The simplest class of operation—reunion of divided arteries or veins—appears to produce no structural alteration of note beyond the traumatic effects in the immediate vicinity of the line of suture.

Protocol.

May 7.—Dog 21: young adult, black, male. Weight, 6·3 kilogrammes. Under ether anæsthesia both common carotid arteries were divided, and the central end of the left was anastomosed to the peripheral end of the right; twenty-five stitches and twelve minutes were required for the operation. The other end of the arteries were permanently ligated. The right external jugular vein was divided and reunited; twenty stitches and ten minutes were required. The dog made an uneventful recovery.

May 17.—Circulation appeared to be good through both anastomoses.

May 27.—The animal was etherized; after exposing the vessels, and demonstrating that the circulation was excellent, the specimens were removed (Fig. 57).

Protocol.

May 29.—Dog 6: black bull-poodle, male. Under ether anæsthesia the trunks of both common carotid arteries were divided and the ends ligated. A lateral anastomosis near the central

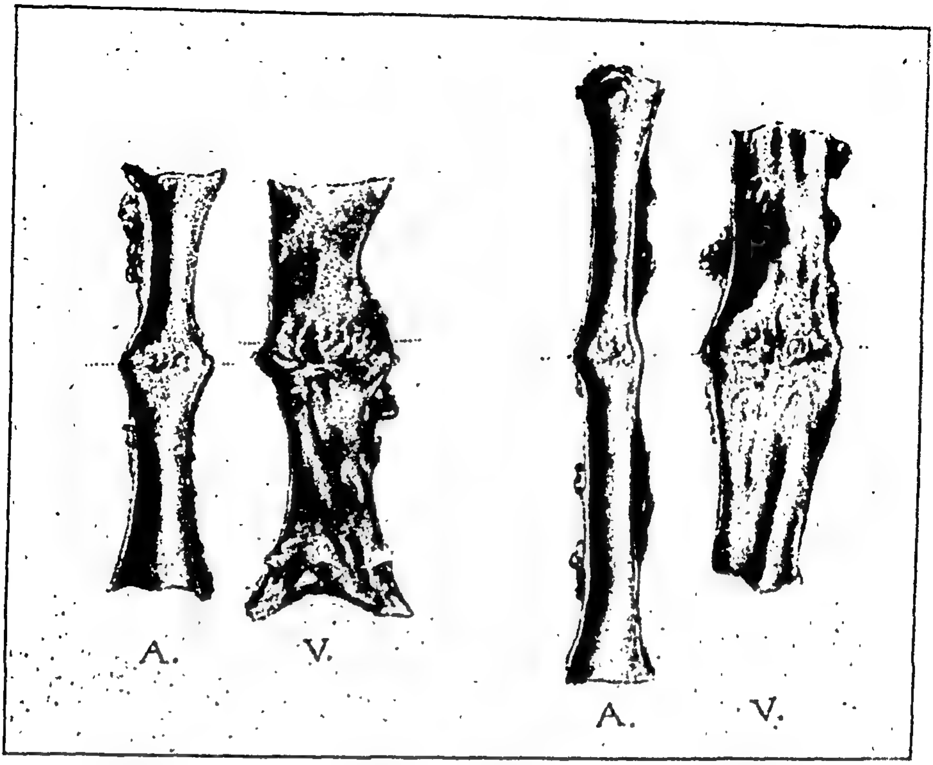


FIG. 55.—CIRCULAR SUTURE OF BOTH CAROTID ARTERIES AND BOTH JUGULAR VEINS, FORTY-ONE DAYS AFTER OPERATION. (WATTS.)

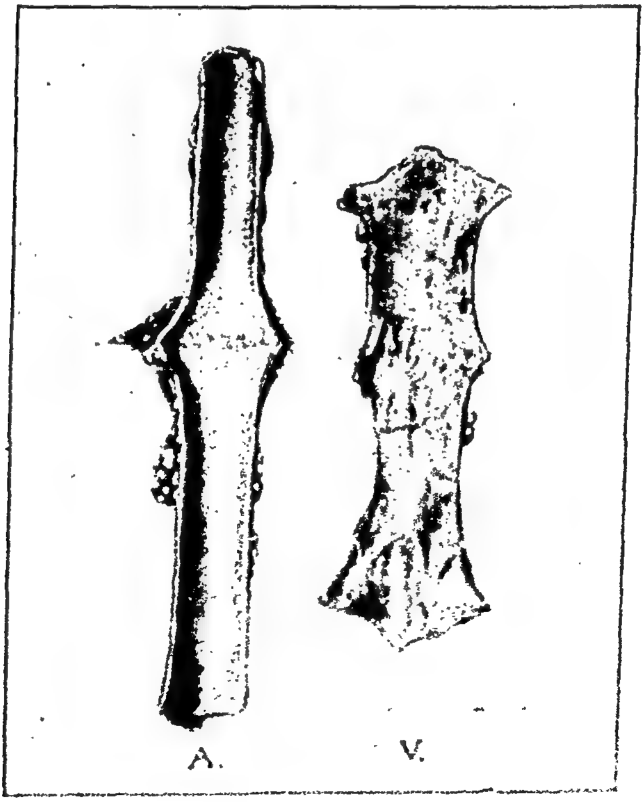


FIG. 56.—CIRCULAR SUTURE OF CARTOID ARTERY AND JUGULAR VEIN, FORTY-EIGHT DAYS AFTER OPERATION. (WATTS.)

end of the left and near the peripheral end of the right, was instituted (Fig. 58).

December 19.—The animal was etherized; the circulation through the anastomosis was seen to be excellent. The specimen was removed. On longitudinal section the intima was smooth and glistening; the stitches were seen beneath it. The lumen was unobstructed.

The results of more complex combinations, the interposition of an arterial segment between the ends of a divided artery, and the interposition of a venous segment between the ends of a divided artery are illustrated by the figures, and are described below.

Protocol.

April 24.—Dog 18: old black-and-brown male cur. Weight, 9 kilogrammes. Purulent discharge from nose. Etherized.

Removed segments of the left external jugular vein, the right common carotid and left common carotid arteries. Inserted a segment of the left external jugular vein between the cut ends of the right common artery. Transplanted the segment of the right common carotid artery between the ends of the left common carotid artery.

April 28, *p.m.*—The dog was very weak, and there was much discharge from the nose. He would not eat or drink. The bowels were loose.

April 29, *a.m.*—Dog died.

At post-mortem examination the wound was dry and well healed. The deep neck sutures were in excellent condition. The right common carotid artery and the venous segment were in good condition, as were also the left common carotid artery and the segment of the right common carotid artery (Fig. 59). Opened thorax. Advanced purulent pericarditis, with pleural effusion, were present. A large quantity of purulent liquid was found in the pericardial and pleural cavities. The pericardium was enormously thickened.

Protocol.

April 29.—Dog 20: medium-sized adult dog. The common carotid arteries were exposed under ether anæsthesia. A small segment from the left was removed and preserved. A segment from the right was removed and interposed between the ends of the left. The right external jugular vein was exposed, and a segment removed

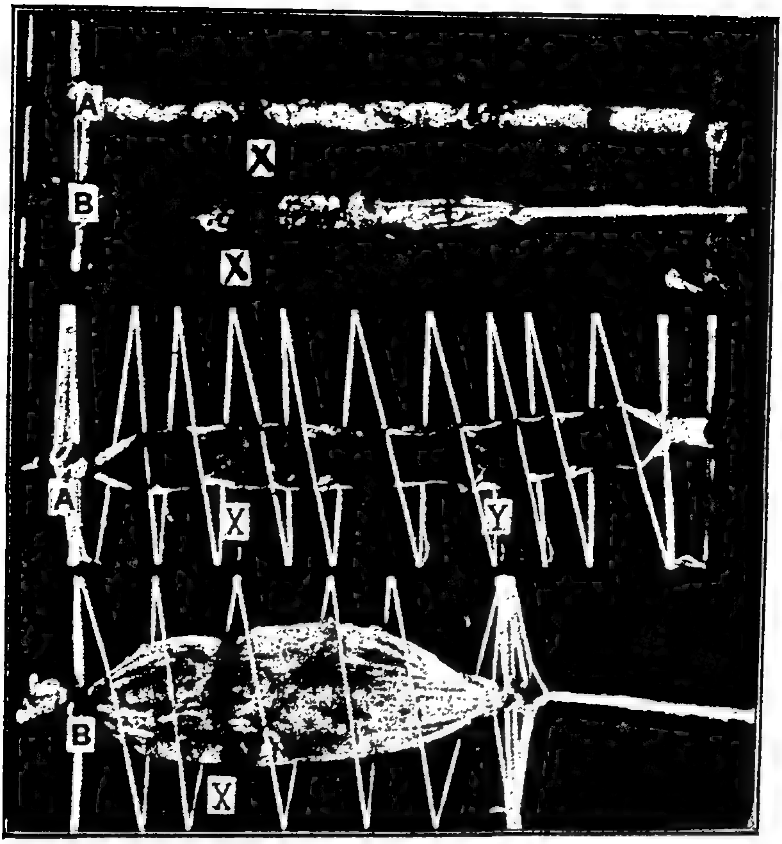


FIG. 57.—ANASTOMOSIS OF—A, CAROTID ARTERY TO CAROTID ARTERY; B, JUGULAR VEIN TO JUGULAR VEIN, TWENTY DAYS AFTER OPERATION, EXTERNAL AND INTERNAL SURFACES.

X indicates line of anastomosis. Y indicates another line of anastomosis made the day before the animal was killed. (Dog 21.)

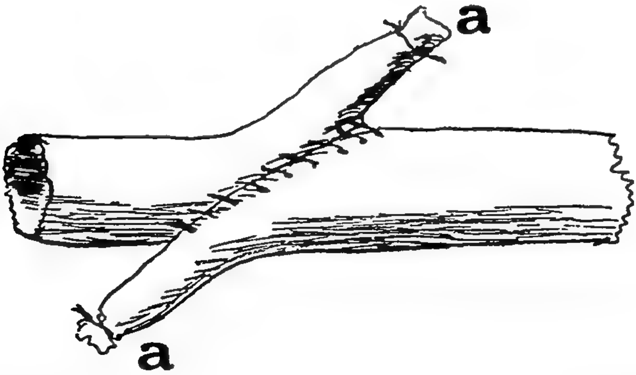


FIG. 58.—TERMINO-LATERAL ANASTOMOSIS OF CAROTID ARTERIES.

Diagram of the union of the vessels seven months after the operation. a, a, ends of arteries ligated. (See also Fig. 54.)

and interposed between the ends of the right common carotid artery. The normal direction of the circulation in both segments was preserved. Very little sodium chloride (0·9 per cent.) solution and paraffin-oil were used. The circulation through both segments was excellent. The dog made an uneventful recovery.

May 12.—The circulation on both sides was excellent.

May 21.—The circulation on both sides was excellent.

May 27.—The carotid arteries were exposed, and a very active circulation through the segments was demonstrated. The specimens were removed (Fig. 60).

The arterial segment showed no marked changes except at the lines of anastomoses. With the venous segment the case was quite different, especially after some weeks, when it showed not only moderate and somewhat irregular thickening, but marked histological alteration.

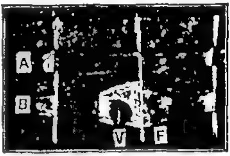


FIG. 59.—A, SEGMENT OF CAROTID ARTERY ON CAROTID ARTERY; B, SEGMENT OF JUGULAR VEIN ON CAROTID ARTERY, FIVE DAYS AFTER OPERATION.

V, indicates valve into the pocket of which a half-circular piece of black paper was inserted before photographing. F, indicates small lamellar white fibrinous deposit. (Dog 18.)

Macroscopically, the venous segment was of about the same size, or perhaps a little larger, than when last seen. Externally, it was fibrous and red, particularly in certain areas. Small circular ridges marked the points of anastomoses. On longitudinal section it collapsed. Two sets of valves, which appeared normal, were present, one set being near the distal end of the segment. In physical character the wall was pliable, but somewhat thickened, especially in the intervalvular regions. In the thicker areas it was opaque, while behind the valve-cusps it was quite transparent, and showed little if any thickening. The thickened areas were red, and were richly supplied with blood-vessels, while the thinner and more transparent areas showed slight or no evidence of such vessels. The intima was smooth and glistening throughout, and was continuous with that of the artery at either end. The stitches could be seen at the lines of anastomoses, but they were buried by a covering of newly-formed tissue in all respects similar to the surrounding intimal tissue. The surface presented a somewhat yellowish colouration. The mouths of a

number of small venous branches, which were ligated at the time of the operation, appeared.

Microscopically, besides an irregular thickening, the most striking features were evidences of œdema and retrogressive changes of a hyaline character; complete absence of muscle fibres; numerous newly-formed blood-vessels in the outer coats, most marked in the thicker areas; masses of interstitial (extravascular)

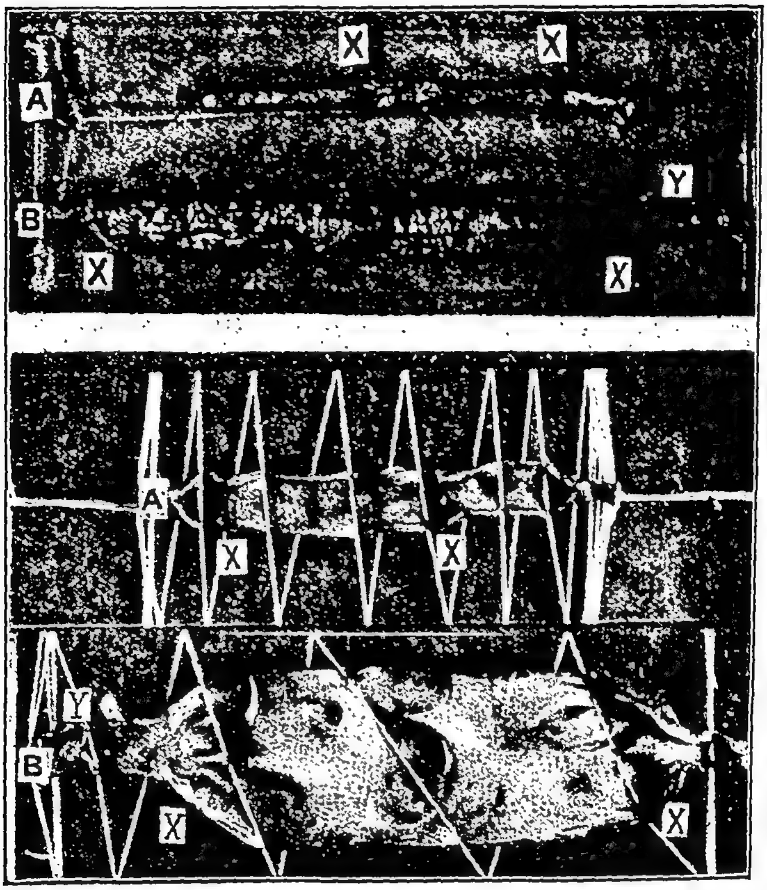


FIG. 60.—A, SEGMENT OF CAROTID ARTERY ON CAROTID ARTERY; B, SEGMENT OF EXTERNAL JUGULAR VEIN ON CAROTID ARTERY, TWENTY-EIGHT DAYS AFTER OPERATION.

External (adventitial) and internal surfaces of artery. X indicates line of anastomosis. (Dog 20.)

blood in the outer coats of the thicker areas; and a very pronounced perivascular (periadventitial) fibrosis. At the lines of anastomoses the appearance was modified by the traumatic effects. The embedded ligature was separated from the lumen by what appeared to be the organized remains of a thin, band-like thrombus or fibrinous deposit, which presented a smooth surface, and was composed of flattened cells, with elongated nuclei (Baumgarten type of cells).

The superficial cells, though not identical in appearance with those of normal intimal endothelium, resembled them in general character and arrangement. Elastic fibres, which were fairly abundant, were chiefly of the coarser variety. For the most part they were longitudinally arranged, and occurred in the inner coats, and especially in what corresponded to the middle coat normally. The circularly disposed fibres were situated internally to the longitudinal ones.

Attention is called particularly to the fact that muscular hypertrophy was not observed, which is opposed to the observations of Watts, and to the more recent observations of Fischer and Schmieden, who reported an augmentation in muscular elements, both in size and numbers. But Watts did not especially study such changes, as he was investigating primarily the larger problem of the feasibility of vascular anastomoses. On the other hand, Fischer and Schmieden devoted special study to the matter. Also it should be noted that the writer's studies indicate that the muscular tissue of a segment of vein engrafted between the ends of a divided artery progressively decreases. This indicates that a certain time is required for the disappearance of such tissue failing to survive. And since the disappearance of a tissue after death is due to disintegrative and absorptive processes, and since the absorptive mechanism is no doubt thrown out of gear, owing to the interruption of the circulation in the capillaries of the vascular wall, such a result would be anticipated. This point very probably would do much in explaining the persistence of muscular tissue in engrafted vascular segments for considerable periods, and especially in tissues previously treated in such a way as to destroy or greatly lower their vitality as preservation in formaldehyde solution or cold storage. And to demonstrate the force of the argument, it is only necessary to observe the long time required for the disappearance through absorptive process of a thread of catgut introduced into the tissues.

Hetero-Transplantation.

A segment of rabbit's aorta interposed between the ends of a divided artery of a dog, though performing an adequate function as regards the transmission of blood, showed marked changes. A similar result was observed in an aortic segment from a cat similarly engrafted into a dog.*

* *American Journal of Physiology*, 1907, xxx. 482.

Protocol.

May 15.—Dog 2 : young adult, female, in fair condition. Weight about 11·3 kilogrammes. Large double goitre. A segment of the left common carotid artery, 0·5 centimetre long, was removed, and a segment of the abdominal aorta from a 3,000 grammes white, male rabbit was interposed, the segment being about 2·5 centimetres long. The arteries of the dog were considerably enlarged. The diameter of the common carotid artery was more than twice that of the engrafted aortic segment. The circulation was restored through the segment about one and a half hours after its removal from the rabbit.

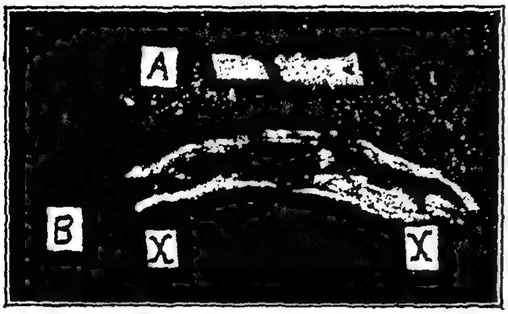


FIG. 61.—TRANSPLANTATION OF RABBIT'S AORTA ON DOG'S CAROTID ARTERY—A, AS AT TIME OF TRANSPLANTATION; B, SEVEN MONTHS LATER.

A portion of A was removed for histological examination.

June 15.—Under ether anæsthesia the wound was reopened, and the segment of aorta was found to have the same diameter as the carotid artery, and to be somewhat longer than at time of transplantation. The circulation was excellent.

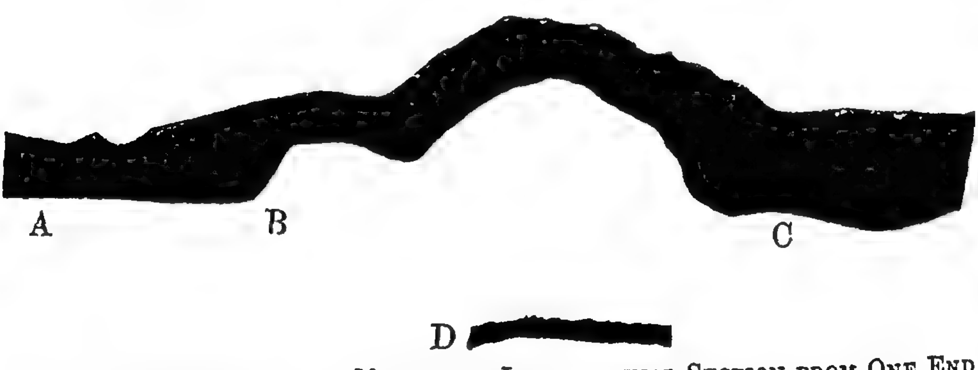


FIG. 62.—PHOTOGRAPH OF A MAGNIFIED LONGITUDINAL SECTION FROM ONE END OF THE SPECIMEN SHOWN IN FIG. 61.

A, end of dog's common carotid artery; B, beginning of rabbit's aortic segment; C, strongly calcified area. *A fracture of tissues occurred at this point* (very probably an artifact). Also there was a comparatively large space near the middle of the wall, apparently empty at this time. D is a longitudinal section of normal rabbit's aorta, mounted, sectioned, and stained with the engrafted specimen, and photographed under the same magnification.

December.—The transplanted segment was removed. The circulation at the time was excellent.

Macroscopically, the segment was much enlarged. It was greyish in colour, and densely fibrous in appearance. It was quite rigid, and on longitudinal section, which procedure indicated a considerable degree of calcification, the walls showed no tendency to collapse. Separation of the longitudinal edges was resisted by the rigidity of

FIG. 63.—DOG, BETWEEN THE ENDS OF WHOSE DIVIDED COMMON CAROTID ARTERY (RIGHT) A SEGMENT OF FORMALDEHYDE FIXED VENA CAVA OF ANOTHER DOG WAS ENGRAFTED.

The artery still pulsates, and the animal is in excellent condition more than three *years after the operation.*

the walls, and on forcing the artery open, rupture of the intimal surface occurred at the point of greatest extension. Except for this, the intimal surface was smooth and glistening, though presenting several cup-like irregularities, which were neither very abrupt nor deep. The intimal surfaces of the segment and of the artery at either end were continuous and smooth. The wall was

somewhat irregularly transparent. The lumen was much larger than that of the artery.

Microscopically, the wall varied in thickness from about three to six times its thickness at the time of transplantation. The intimal surface was smooth, and continuous with that of the artery. The tissues were stained irregularly and diffusely (hæmatoxylin eosin). They were densely fibrous, and showed retrogressive changes of a hyaline character and areas of calcification.

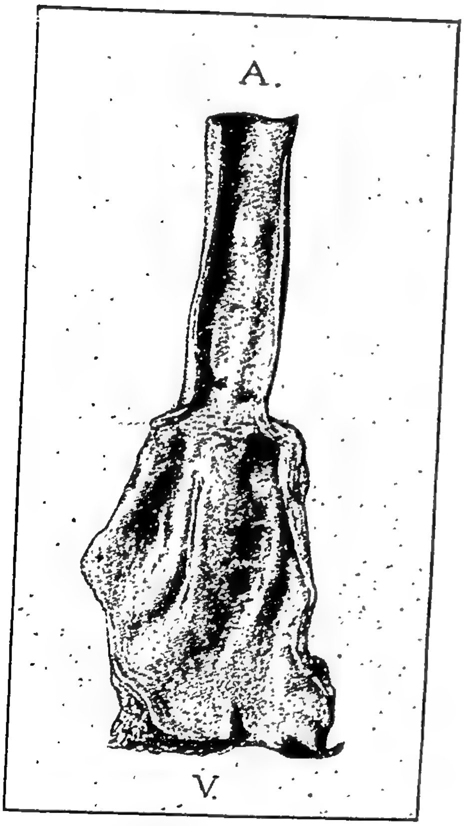


FIG. 64.—CIRCULAR ANASTOMOSIS OF FEMORAL ARTERY AND VEIN, THREE MONTHS AFTER OPERATION. MARKED THICKENING AND DILATATION OF VEIN. (WATTS.)

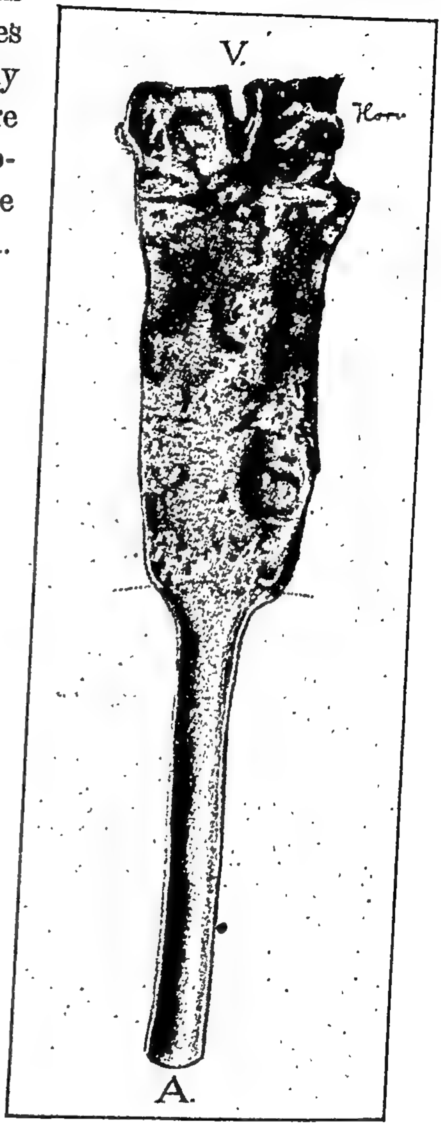


FIG. 65.—CIRCULAR ANASTOMOSIS OF CAROTID ARTERY AND JUGULAR VEIN, THREE MONTHS AFTER OPERATION. MARKED SCLEROSIS OF VEIN. (WATTS.)

No muscle was present. The suture material was deeply buried at the lines of anastomoses. From near this point (line of anastomosis) the ends of the carotid artery appeared normal.

A segment of vena cava was taken from a dog, and preserved and fixed for sixty days in 2·5 per cent. formalin in 0·9 per cent. sodium chloride. It was treated with dilute ammonia, dehydrated in absolute alcohol, and impregnated with paraffin-oil, and then engrafted between the ends of a divided common carotid artery of

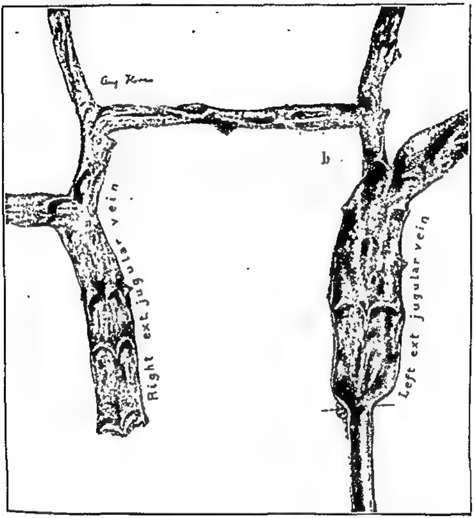


FIG. 66.—CIRCULAR ANASTOMOSIS OF THE LEFT COMMON CAROTID ARTERY AND LEFT EXTERNAL JUGULAR VEIN, FOUR MONTHS AFTER OPERATION. (WATTS.)

As a result of the arterial pressure, this vein is much thickened and dilated. Small branch of vein occluded (b) probably due to valves, being forced together and becoming adherent.

another dog. Excellent functional restoration was observed. Twenty-three days after the operation direct examination (under anæsthesia) revealed an excellent circulation, confirming the previous clinical examination, and the segment, though it showed some alteration, was performing its function well (p. 130). More

than three years have elapsed, and the carotid pulse is normal. Histological studies have not been made (Fig. 63). According to Levin and Larkin, who later reported similar experiments, considerable structural alteration should occur. But since their longest observation, uncomplicated by occluding thrombosis, was of but eleven days' duration, and was complicated by infection, the observation of ultimate structural results are still wanting. And their criticism of Carrel's views regarding the survival of tissues in hetero-transplantations, and of similar transplantations of tissues preserved in cold storage, though warranted from a theoretical standpoint, as I pointed out some years ago,* are not fully borne out by their experiments.†

Simple arterio-venous anastomosis, as in arterialization and reversal of the blood-stream in the distal end of a vein by uniting it with the central end of an artery, is followed by marked structural changes in the vein (*cf.* Figs. 64, 65 and 66).

Protocol.

June 15, 1907.—Dog 4: young adult, female. Good condition. Weight, 11·3 kilogrammes. Presents a large symmetrical and double goitre.

Under ether the circulation was reversed in the right inferior thyroid vein by dividing and anastomosing its peripheral end to the central end of the divided right common carotid artery. The subsequent circulation was excellent. The thyroid immediately became engorged, and showed strong pulsatory expansion and contraction, and commencing œdema. The wound healed rapidly, and the animal remained in good condition.

May 12, 1908.—The blood-vessel was re-exposed under ether and removed.

Macroscopically, the vein was somewhat larger in diameter, and the walls more rigid and thicker than normally. In colour it was pale and greyish. No marked vascularity was noted. Upon longitudinal section it did not collapse. The intima was smooth and glistening, and continuous with that of the artery. The actual line of blending of the arterial and venous tissues could only be detected by close examination. The wall appeared to be abnormally transparent.

Microscopically, the wall was thickened. The intima was smooth,

* *Journal of the American Medical Association,* 1908, l. 1035.

† *Cf.* Klotz, *Science,* 1911, N.S., xxxiii. 899.

and beneath it there was muscular tissue, though not an abundance of it. The remainder of the wall was dense, hyaline, and fibrous in character, and very few nutrient blood-vessels could be seen. The fibrosis was most marked external to the middle coat. In the latter was a moderate number of elastic fibres, chiefly of the longitudinal coarser type.

Experiment showing Results of Arterio-Venous Anastomosis after more than Five Years.

Dog O.—Made anastomoses between central end of the right common carotid and the peripheral end of the right external jugular vein, and the peripheral end of the right common carotid artery and the central end of the right external jugular vein.

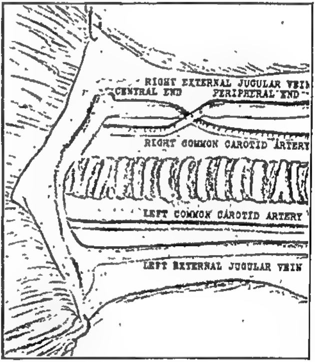


FIG. 67.—SHOWING OPERATION PERFORMED ON DOG O. (See text.)

The animal made a prompt recovery. Pulse and thrill in peripheral end of the external jugular vein. That the pressure in the vein was less than arterial was indicated by the relatively slight pressure on the peripheral portion of the vein adequate to occlude the lumen, such pressure presumably being applied distal to anastomotic branches. By palpation it could be demonstrated readily that the pressure in the peripheral end of the external jugular vein was greater than in the unoperated vein. The animal remained in excellent condition, and gave birth to three litters of pups. More than five years after the operation the animal was killed in a fight with other dogs. At the last observation, sixteen days prior to death, the circulation was excellent. The day preceding death the animal was in good condition. At post-mortem examination the vessels were exposed by a medium incision down to the trachea.

Clotted blood was found in and between the subcutaneous and deeper tissues, but especially in the carotid sheath. The carotid artery on the operated side was found and traced to where it passed out through the neck muscles. It was strongly adherent to the muscular fascia at the point of exit. The point of anastomosis was at or near the point of adhesion. On opening the vessel longitudinally, the line of anastomosis was located by the lighter colour of the intima on the arterial side. By holding the specimen in a good light it was possible to make out about twelve slight longitudinal markings that in position correspond with the position of the stitches. The intima on the venous side was smooth, but the surface somewhat corrugated, due probably to the puckering of the vein necessary in order to reduce it to the size of the artery at the point of anastomosis. A few millimetres above the line of anastomosis a small pear- or heart-shaped mass was seen projecting slightly into the lumen of the vessel. It was continuous above with the wall, but the narrow portion directed downward was free. Passing the blade of a small pair of dissecting forceps upward beneath the free extremity, the point emerged through an opening near the centre of the attached portion. This channel no doubt transmitted blood during the life of the animal, and together with the free point projecting into the blood-stream was probably concerned in the production of the marked thrill which was so pronounced in the circulation in the peripheral end of the vein. The central end of the artery below the anastomosis was much more elastic than the peripheral end of the vein above the anastomosis. At the point of anastomosis a ridge was felt.

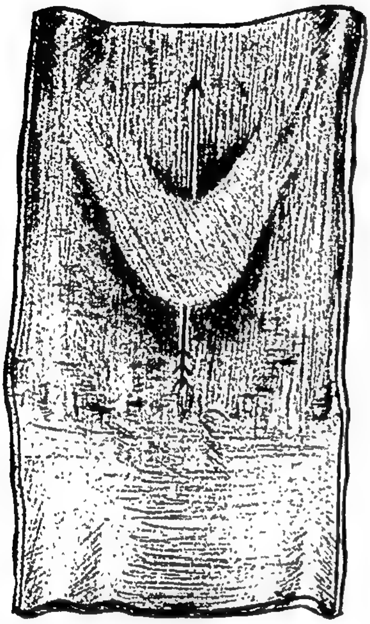


FIG. 68.—SHOWING LINE OF ANASTOMOSIS BETWEEN THE CENTRAL END OF THE RIGHT COMMON CAROTID ARTERY AND THE PERIPHERAL END OF THE RIGHT EXTERNAL JUGULAR VEIN AFTER FIVE YEARS (DOG O). ALSO SHOWS REMAINS OF VALVE IN VEIN.

The arrow indicates the opening through the valve flap, and also the direction of the blood-stream.

The line of anastomosis between the peripheral end of artery and central end of the vein was discovered by feeling a rather hard mass about the size of a pin's head. On opening the vessel longitudinally

this was found to be a localized thickening of the wall, due probably to puckering of the vein. The ligature was seen at this point beneath the intima, which was smooth and glistening.

The extensibility and elasticity of the vein below the anastomosis, tested by stretching with the fingers, was greater than that of the vein on the opposite side, but a little less than that of the artery above the anastomosis. The elasticity of the artery above the anastomosis

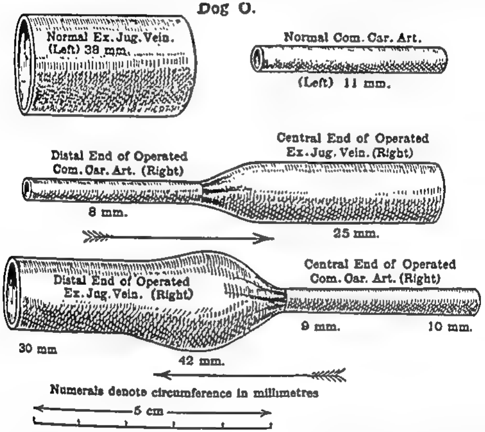


FIG. 69.—SHOWING RELATIVE SIZES OF BLOOD-VESSELS FOLLOWING ARTERIO-VENOUS ANASTOMOSES MORE THAN FIVE YEARS AFTER THE OPERATION (DOG O).

Numerals indicate circumference of vessels; arrows indicate direction of circulation. Scale in centimetre divisions. (Diameters are drawn about 50 per cent. larger than scale.)

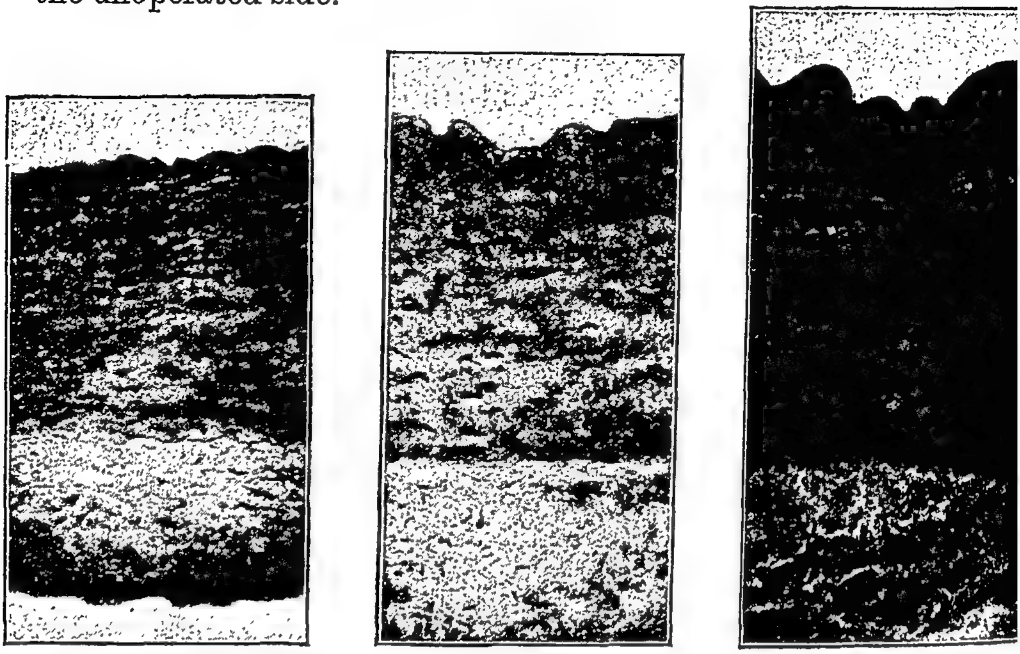
was about the same as that of the artery on the opposite side, but the resistance offered in stretching the artery above the anastomosis was less than the normal artery.

The superior thyroid branch of the normal artery was much larger than the same branch of the operated artery.

The thyroid lobe on the operated side measured 1·5 by 3·0 centimetres.

The thyroid lobe on the unoperated side measured 1·5 by 4·5 centimetres.

The lobe on the operated side was firmer in consistency than on the unoperated side.



Unoperated Artery. Central End of Operated Artery. Peripheral End of Operate Artery.

Fig. 70.—Relative Thickness of Coats of Arteries of Dog O Five Years after Operation.

Retouched microphotograph. Magnification the same in all. (See Protocol, and Fig. 69).

Measurements of the Walls of the Common Carotid Arteries and External Jugular Veins of Dog O.

	Intima and Media.	Adventitia.	Total Thickness.	Peri-adventitial.
	μ	μ	μ	μ
Normal artery	595·0	357·0	952·0	—
Central end artery	714·0	333·2	1047·2	9·0
Peripheral end artery ..	904·4	333·2	1237·6	—
Normal vein	119·0	238·0	357·0	—
Central end vein	249·9	292·5	542·4	14·0
Peripheral end vein	261·8	404·6	666·4	—

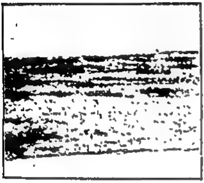
Histological examination gave the following results:

The wall of the unoperated artery appeared normal.

The wall of the central end of the operated artery was slightly thicker, and the lumen smaller, and the intimal surface more corru-

gated than the unoperated artery. The thickening was chiefly medial and periadventitial. The tissues otherwise appeared normal.

The wall of the peripheral end of the operated artery was thicker, and the lumen smaller, and the intimal surface more corrugated,



UNOPERATED VEIN.

CENTRAL END OF OPERATED VEIN.

PERIPHERAL END OF OPERATED VEIN.

FIG. 71.—RELATIVE THICKNESS OF COATS OF VEINS OF DOG O FIVE YEARS AFTER OPERATION.

(See Protocol and above figures.)

than in the central end. The thickening was chiefly medial; otherwise normal.

Quantitatively, the cross-sectional area of the muscular tissue of the media of the peripheral end of the operated artery was not increased, although the thickness of the medial was increased.

The wall of the unoperated vein appeared normal. The lumen may have been somewhat enlarged owing to the increased functional demands made upon it.

The wall of the central end of the operated vein was thicker and the lumen smaller than the unoperated vein. In structure it was densely fibrous, particularly the adventitial and periadventitial layers. The muscular tissue does not appear altogether normal, but complete studies have not been made.

The wall of the peripheral end of the operated vein is thickened, and the lumen, excepting for a short distance beyond the anastomosis, is smaller than the lumen of the unoperated vein. There is a fibrosis of all the coats, especially of the muscularis and adventitia.

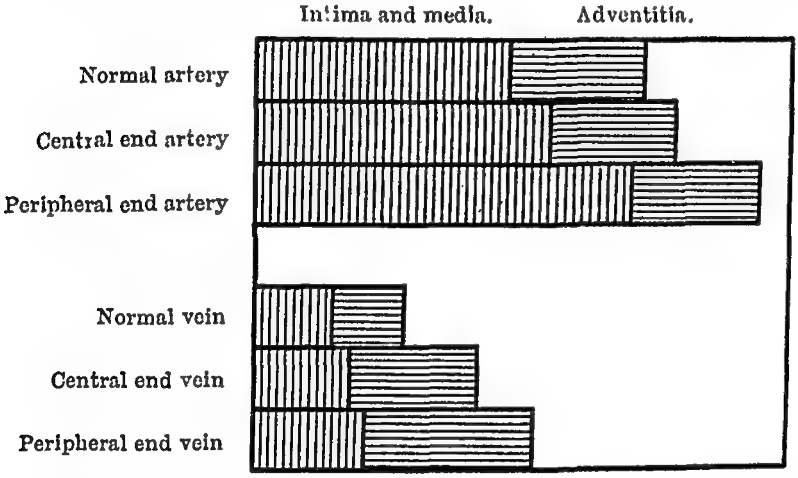


FIG. 72.—SHOWING RELATIVE ALTERATIONS IN THICKNESS OF VASCULAR COATS AFTER CHANGING THE CIRCULATION, FIVE YEARS AFTER OPERATION. (DOG O.)

Central end of artery connected to peripheral end of vein, and peripheral end of artery connected to central end of vein. The diagram was not constructed from the identical measurements given in the table on p. 98.

The muscle fibres are pale, and the layers are widely separated by fibrous tissue. The fibrous tissue has a less band-like arrangement, and is more homogeneous than in the central end of the vein.

Summary.

1. Union of arteries or veins, either end-to-end or by lateral openings, by through-and-through suturing as described, is not followed by structural alterations of note in the vessels themselves, excepting for the insignificant traumatic effects at the line of union.

2. In veins in which the circulation is changed to arterial and reversed, thickening is observed. Muscle tissue has been observed after five years. In the central end of a common carotid artery anastomosed to the peripheral end of an external

jugular vein, no very marked changes in the size compared to the *unoperated companion vessel nor in the coats are observed after five* years. In the central end of an external jugular vein anastomosed to the peripheral end of a common carotid artery more than five years, *a decrease in the size and an increase in the thickness of the wall* was noted; while the peripheral end of the artery is considerably decreased in size, and the wall is thicker, and the intima more corrugated, than in the unoperated companion vessel.

3. Eck's fistula in cats is not followed by vascular changes of note. Of additional interest is the observation that cats, during one and two years respectively, showed absolutely no clinical abnormalities even on an exclusively meat diet. This is at variance with the statement commonly made for dogs, the latter generally showing symptoms similar to ammonia intoxication (convulsions), said to be due to the incomplete conversion of the nitrogenous end-products of protein metabolism into urea, etc.

4. A segment of dog's carotid artery removed, and quickly engrafted between the cut ends of the other common carotid artery, after four weeks shows very little microscopic change, excepting for some thickening at the line of anastomosis.

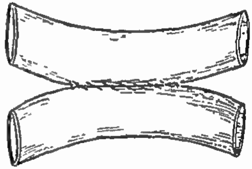


Fig. 73.—Diagram of Lateral Anastomosis (Eck's Fistula) between Two Blood-Vessels.

5. A segment of a dog's external jugular vein removed and quickly engrafted between the ends of a common carotid artery, the normal direction of blood-flow being preserved, after four weeks shows moderate thickening and indications of degeneration, particularly of the muscular tissue. A similar segment after five days shows much less change.

6. A segment of dog's external jugular vein removed and treated with salt solution, and engrafted between the ends of a common carotid artery, at the end of two weeks shows very much greater thickening than in the result above cited, but muscular tissue is present.

7. A segment of rabbit's aorta engrafted between the cut ends of a dog's common carotid artery, after seven months shows great enlargement, and enormous thickening and hardening (calcification) of the walls. Muscular tissue is absent.

8. A segment of dog's vena cava, preserved for sixty days in 2·5 per cent. formalin, then washed in dilute ammonia, dehydrated with absolute alcohol, impregnated with paraffin-oil, and then trans-

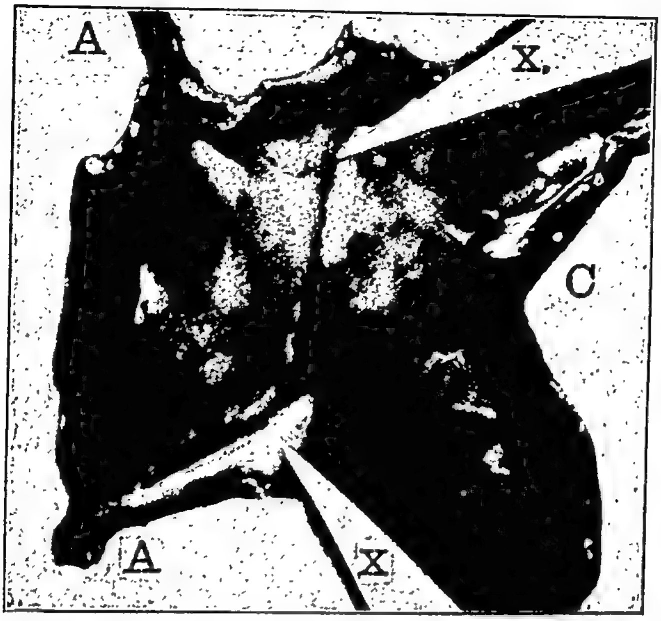


FIG. 74.—RESULT OF LATERAL ANASTOMOSIS BETWEEN THE PORTAL VEIN AND VENA CAVA (ECK'S FISTULA) OF A CAT AFTER MORE THAN A YEAR.

A, A, Ends of portal vein; C, vena cava. Specimen is laid open, showing smooth intimal surface. The line of anastomosis is indicated by the pointers, marked X, X.

planted between the ends of a common carotid artery of a bitch, three weeks ofter the operation shows an active circulation, but marked enlargement. After more than three years the pulse in the artery is still good.

Discussion of Structural Alterations observed in Blood-Vessels after Vascular Operations.

It might be anticipated that such experiments would cast some light on the nature of the processes resulting in the pathological conditions of similar anatomical character observed in blood-vessels—*e.g.*, arterio-sclerosis. Indeed, a considerable number of statements from this view-point have already appeared in the literature. I may here be permitted to recall attention to the early statements of Carrel and myself on this phase of the subject, and to my later statement calling attention to the complexity of the factors concerned in such observations. But I shall now show that notwithstanding the soundness of the theoretical considerations,

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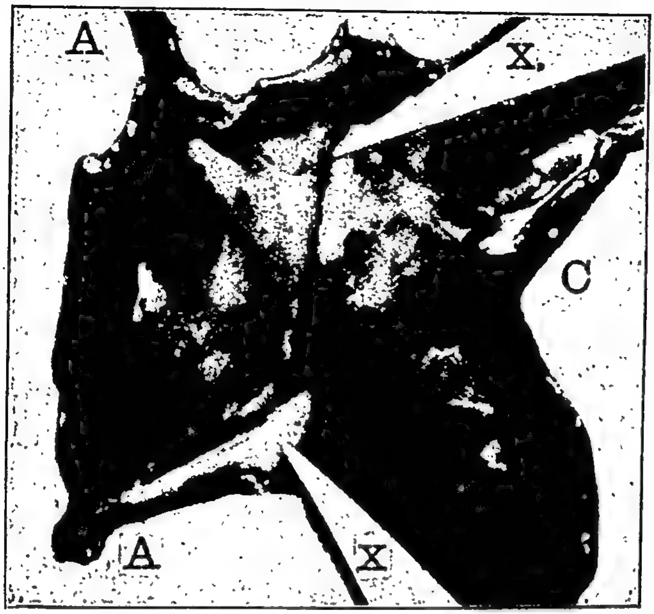

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the information gathered up to date unfortunately does not distinctly advance our knowledge of such pathological processes.

The anatomical changes observed in transplanted blood-vessels having been described, it will suffice to say that they vary extremely. For example, rapidly-made autografts may show but slight structural changes, while heterografts similarly made may show great changes—so great, in fact, that the normal morphological and histological characters may largely disappear. Autografts made with tissues exposed to the prolonged action of harmful agents, such as salt or formaldehyde solutions, show similar alterations, the degree of such change apparently bearing a close relation to the degree of harmful influence to which the tissues have been exposed.

Other factors, such as character of the blood and direction of the blood-stream, alterations in the blood-pressure, and discontinuity of lymphatic and nervous connections, though perhaps not without influence, probably are of a lesser magnitude of importance in determining such structural changes. This applies particularly to the character of the blood, the direction of the blood-stream, and the discontinuity of lymphatic connections. Lastly, the interruption of the nutrient blood-channels, the vasa vasorum, very probably introduces a factor of appreciable magnitude. These factors will be taken up *seriatim*, and discussed more or less in detail.

Physiological Considerations.—The explanations of the structural changes observed in engrafted and in anastomosed blood-vessels are essentially physiological. It is seen in certain cases that certain tissues—*e.g.*, inner intimal cells—may present more or less normal characters, while others—*e.g.*, muscle—wholly disappear. Between these extremes one finds various degrees of normality of the tissues. There is an increase in certain tissues—*e.g.*, fibrous. Now, these differences are due, no doubt in part, to differences in situation. For example, it is said by pathologists that the endothelial cells of the intima are able to carry out their metabolic processes adequately directly with the blood in the lumen of the blood-vessel, which may be termed "functional blood" in contradistinction to nutritional blood in the capillaries of the vasa vasorum. The exact depth to which such an adequate metabolic commerce between the functional blood and the tissues may penetrate the vessel wall is not known, but perhaps not beyond the deeper tissues of the intima; for, according to Mott, degeneration of the media is often

primarily due to obliteration or obstruction of the vasa vasorum, and consequent defective nutrition of the muscular fibres. Similarly the outermost layer of the wall of the vessel would be in a better position to carry on metabolic processes with the blood in the vessels of adjacent tissues than the deeper middle layer. Since it has been known for a long time that the circumferential elements of tissue masses engrafted by the simple method present evidences of better survival than those more centrally situated, the more marked retrogressive changes in the middle coat of such transplanted vascular segments is not surprising.

Also a possible difference in resistance to the abnormal conditions must be considered. It is well known that *different tissues exhibit different resistances to anæmia*, not only as evidenced by tenacity of preservation of function, but by ability of recuperation of function under resuscitatory measures, and by preservation of anatomical structure. Illustrative of these properties is the picture presented by an animal (cat), in which the arterial circulation to the head is suddenly decreased or entirely shut off (see p. 315). The most highly-developed centres (cerebral) appear to succumb first, as shown by loss of consciousness (also seen in fainting), then eye reflexes, respiratory centre, etc., in the order given, the entire process occupying but a minute or two. The same picture is seen in a head after rapid amputation, as in a fowl's head struck off with an axe. The train of clinical expressions of the passing of the nervous tissues into a state of oblivion (inactivity) is surprisingly constant.

If, after all the clinical evidences of nervous activity have disappeared, the circulation be restored (in the case of anæmia by arterial compression by release of the arteries, or in the case of amputation of the head, by restoring an arterial circulation by perfusion, or by engrafting on to another animal), return of function, as indicated by clinical manifestations (reflex and voluntary movements) may be witnessed. In general, recovery may be said to take place in inverse order to the susceptibility of the tissues to anæmia (asphyxia). If the period of inactivity be not too long, evidences of complete recovery of even all of the highest nervous activities may be seen. If, however, the period of anæmia be prolonged beyond a certain time, only the so-called lower centres—*e.g.*, respiratory—may appear to completely recover, the higher ones showing only partial recovery, or evidences of their recovery may be entirely wanting. Indeed, a condition in cats resembling insanity has been

observed following resuscitation of the brain after a prolonged period of anæmia.

The changes wrought in the cells of the tissues of the central nervous system by asphyxia also point to the conclusion that a relative susceptibility to an adverse condition in the elements of the nervous tissues exists. That such changes occur has long been known, but recently Pike and Gomez (p. 325) have studied the tissues of brains and spinal marrows which had been subjected to varying periods of anæmia, the results of which point most clearly to the conclusion above stated. It may here be remarked that drugs, various abnormal states, and even functional states as fatigue, produce similar cytological changes. And, further, since all these conditions affect the respiration of the tissues, the known tendency in many cases being toward asphyxia, to me these facts are evidences of the correctness of the view that many drugs produce certain clinical symptoms in virtue of properties of interfering with respiratory processes, and that the same is probably true in many pathological and abnormal conditions, not ordinarily attributed to asphyxia.

From this standpoint it would seem that to attribute the primary clinical changes to such cytological alterations (chromatolysis, etc.) is illogical. To illustrate: If an animal's head be struck off, and a bit of tissue from the brain be removed after ten minutes or so, and fixed and examined cytologically, relatively slight evidences of chromatolysis, etc., will be seen as compared to a similar tissue taken from a similar animal after resuscitation from apparent death from a period of cerebral anæmia (asphyxia) of the same length. Now, abnormal clinical symptoms after resuscitation cannot properly be attributed to the cell changes, asphyxia being the primary cause. Indeed, after such treatment such a cell may perhaps remain in a state of asphyxia for a long time, due to an inability to carry out a normal respiration owing to the injury wrought by the primary asphyxiation. Thus the view that much light can probably be thrown on the clinical phenomena following the administration of drugs (poisons), as well as those observed in numerous abnormal and pathological conditions from the standpoint of tissue respiration, seems worthy of further pursuit.

Similarly, *different* tissues show differences in susceptibility to anæmia (asphyxia) and in powers of recuperation. In general, it may be said that the more highly organized and developed a tissue the more delicate it is in this respect. Any such general statement,

however, only roughly approximates the order in which the tissues stand in susceptibility to asphyxia. ✓

More specifically, the more abundant tissues found in segments of arteries and veins probably stand in about the order of nervous, muscular, fibrous, and endothelial as regards susceptibility to anæmia (asphyxia, autolysis, etc.). The basis of the statement for nervous tissue is the common statement that nerves degenerate when cut off from their "trophic centres," and only reappear by an ingrowth from the central tissues. A good illustration of the resistance of the intimal endothelial cells is the discovery of Professor Wells that, subjected to autolytic conditions, the endothelial cells of the intima exhibit the strongest resistance.

Finally, *the regenerative powers of the tissues* have to be taken into account, as a very considerable difference in this respect is known to exist. For example, it is commonly held that in mammals the cells of the central nervous system, and muscle fibres as well, are incapable of regeneration, while epidermal and fibrous tissues exhibit a very marked ability in this respect. Also, fibrous tissue is prone to replace other tissue that has suffered destruction, either by trauma or through retrogressive processes due to numerous agencies. As illustrative of the remarkable proliferative powers of the intimal cells, and of very striking interest in connection with complete biterminal vascular transplantations, is an observation by Professor Adami. He observed a complete intimal lining in an aortic dissecting aneurism which extended from the thoracic to the iliac region, the case presenting a history indicating that the aneurism was of not more than a few weeks' standing.

It is interesting to consider the results observed after simple injury of the intima, as well as intimal interruptions such as occur in vascular anastomoses (p. 58). It will be recalled that these findings show that at a time when the reparative processes have resulted in the gross appearance of intimal repair (lamellar white thrombi), microscopical examination shows that the newly-laid-down materials are not identical in appearance with normal intimal endothelium. Indeed, it is shown by the occurrence of non-occluding thrombi that abnormal surfaces may simulate an intimal surface in being smooth and glistening, and in being at least inert in so far as inducing fibrin deposition from living blood in contact with its surface is concerned. An observation by Guthrie in 1830 is interesting. The left subclavian artery was closed at its origin by a coagulum, leaving a channel through the centre for the blood-

stream. The canal in the coagula seemed smooth, as if lined by a false membrane. The question naturally follows, May the tissues of non-intimal origin assume the general character, and functionate adequately in place of a normal intimal surface? Or is such restitution of intimal continuity achieved by the ingrowth of neighbouring intima, or by the outgrowth or penetration of intimal tissues through the fibrinous deposit from the bottom of the wound? Although, as I am fully aware, the latter two views are the more orthodox, I am as yet unconvinced of the impossibility of tissues of other than intimal origin assuming such a function by an adaptive differentiation. According to Hektoen, a thrombus is regarded as an absolutely dead mass, and in reorganization replacement fibrosis takes place from the vessel wall.

The character of the blood circulating in an engrafted segment or anastomosed blood-vessel may have an influence in determining the resulting structural changes. For example, a vein may be caused to carry arterial, and an artery venous, blood (p. 157). Since, as before stated, the tissues near the intimal surface are said to take nourishment from the blood in the lumen of the vessel, such alteration of the blood may be an appreciable factor in the results; normally the metabolism of such tissues in veins may be considered as attuned to venous blood, and such tissues in arteries attuned to arterial blood. In the former case, arterial blood would at first sight appear to favour greater activities on the part of such tissues, but this cannot be considered as established until more data are obtained. The mere carrying of more blood to a part, or the better arterialization of blood, is not necessarily followed by increased activity on the part of the affected tissues. Indeed, there is evidence that the opposite condition, a condition similar to a state usually considered as peculiar to the pulmonary respiratory mechanism, termed "apnœa," which is observed best after a hyperoxygenation of the blood, together with a decreased content of carbon dioxide, as after a period of rapid pulmonary ventilation, may result. On the whole, the theoretical evidence is much stronger that tissue normally supplied abundantly with arterial blood—*e.g.*, an artery—would probably be more affected by causing the blood-supply to become venous. The results of the arterialization of the circulation in a vein are given on p. 95 (Dog O).

Direction of the blood-stream is a possible factor in the results. But excepting for the valves in veins, no strong argument either for or against the view can, so far as I am aware, be decisively supported at the present time.

Alteration of blood-pressure is a factor of great interest, not only in the interpretation of structural alterations in operated vessels, but also when considered in connection with sclerosis and related conditions often found in blood-vessels. In the case of a segment of a large vein engrafted between the ends of a divided artery, the pressure in the segment is greatly and continuously increased. For the maximum pressure in a vein, such as the external jugular, as a rule is not more than the equivalent of a few millimetres of mercury, while the pressure in such a vein engrafted upon a large artery, such as a common carotid, is increased perhaps more than twenty-fold.

The resulting structural changes observed in such a segment have already been described, so it will be enough to say that, compared to a similar venous segment engrafted between the ends of a divided vein, the changes appear to be much more pronounced, though it must be stated that a sufficient number of exact observations on the latter operation are as yet wanting. But enough is known to warrant the conclusion that structural alterations suffered by a venous segment on an artery are the more marked.

An analysis of the physical factors resulting from such an increase in pressure in the lumen of the vein is interesting. First, the tissues of the wall are subjected to an abnormal strain, but since of comparable veins and arteries the veins are said to be capable of withstanding as great or greater hydrostatic pressure than arteries, no fears need be entertained as to the adequacy of the veins in withstanding the arterial pressure without danger of rupture. The relatively great pressure subjects the tissues to an abnormal strain, and, although physically adequate, the ultimate effect of such strain on the tissues is problematical. Professor Adami regards the thickening of the wall of such a venous segment as due to strain hypertrophy. But if I understand his interpretation rightly, in the light of the results stated earlier I cannot accept this view. For the hypertrophy meant is in the nature of an active process, the physiological (non-inflammatory) response of the tissues to an increased functional demand, resulting in an abnormal development of the tissue elements. As he puts it, "moderate increase in the work which a tissue is called upon to perform is followed by overgrowth of that tissue, whereas excessive work is followed by rapid exhaustion and atrophy."

Now the question arises, Can the increased work thrown upon the transplanted venous segment (ignoring the pernicious influences

of anastomosis (a point on which I am by no means certain), the the condition in the nutritional vessels of the vein (vasa vasorum would theoretically approximate hyperæmia of the vein, as whe an inferior thyroid vein is ligated, divided, and the periphera end anastomosed to the central end of the opposite commo carotid artery (*cf.* p. 166). And the histological findings in such vein in certain respects bear a striking similarity to the findings i the case of the thyroid gland after such an operation as the on described—namely, a fibrosis consisting of densely packed fibres. Since theoretical explanations are elsewhere offered in explanation of the changes observed in the tissues of thyroid lobes thus operated upon (p. 187), and since the same consideration probably hold, with but slight modifications, for veins, it wi suffice to say that the condition probably results in the productio of partial asphyxiation under the influence of which the processe resulting in the structural changes described occur, the processe thus set up apparently being self-limiting.

Severance of nervous connections is a factor possibly contributin to the results, for it is well known that certain tissues underg structural modifications after section of the nerves going to a part This seems attributable not only to the loss of impulses throug which certain functional mechanisms are thrown into activity o are governed, but also to the causing of nutritional disturbances, largely, perhaps, through alterations in the circulation.

Several authors claim to have obtained positive arterial lesions o a character of arterio-sclerosis by irritating or severing the nerves of the legs, but in each case the influence of the trophic inflammatory disturbances extending from ulcers about the limbs cannot be excluded (Klotz).

To be brief, I may say that no direct evidence has been obtained that nervous connections with an engrafted segment are formed. But special methods of investigating this subject have not been employed. It is, I think, reasonable to suppose that nerves very probably penetrate such tissues along with new blood-vessels, and as the latter may occur in abundance, from this standpoint it may be said that at least certain kinds of nerve fibres very probably grow into such engrafted vascular segments.

Under optimum conditions, as when an arterial segment is removed and immediately replaced, it would seem probable that a very complete re-establishment of nervous connections may occur. But in those cases where great degenerative and structural altera-

tions occur, it is highly doubtful if very extensive nervous connections are formed, as in heterografts or grafts made with dead tissues. In these cases major contractile tissues—*e.g.*, the muscularis—may be entirely absent, so, even though a very complete nervous mechanism develop, which is improbable, certain kinds of fibres would no doubt disappear through degenerative (functional atrophic) processes.

Other factors, such as the toxicity of the host's blood for the graft, as in hetero-transplantations, receive attention in the following chapter.

From the considerations above set forth, I am of the opinion that, basically, the structural alterations noted in engrafted vascular tissues are the expression of the sum total of a considerable number of factors, all of which primarily act through affecting the nutrition of the tissue. Also, that the changes observed so far are, on the whole, of passive, rather than of active, origin, and there is no evidence in any instance that a true functional hypertrophy may occur in such engrafted vascular segments.

REFERENCES.

ADAMI: Inflammation (Macmillan), 1909.

CARREL: C. R. de la S. de B., 1907, lix. 1173; Jr. of Exp. Med., 1907, ix. 226.

CARREL AND GUTHRIE: S. G. and O., 1906, ii. 266.

CRILE AND DOLLEY: Jr. of Exp. Med., 1906, viii. 713.

FISCHER AND SCHMIEDEN: Frankfort Zeitschrift f. Path., 1909, iii. 8.

GOMEZ AND PIKE: Jr. of Exp. Med., 1909, xi. 257.

GUTHRIE, C. C.: Am. Jr. of Phy., 1907, xix. 482; Interstate Med. Journ., 1908, xv., No. 6; Jr. of the Am. Med. Assoc., 1908, l. 1035; Heart, 1910, ii. 115; Soc. for Exp. Biol. and Med., 1909, vii. 45; Science, N.S., 1908, xxvii. 473.

GUTHRIE, C. C. AND F. V.: Jr. of the Am. Med. Assoc., 1910, liv. 340.

GUTHRIE AND RYAN: Interstate Med. Journ., 1911, xviii. 167.

GUTHRIE, STEWART, AND PIKE: Jr. of Exp. Med., 1908, x. 371.

GUTHRIE, G. J.: On Arteries (Maclachlan and Stewart), London, 1830.

HEKTOEN AND RIESMAN: Am. Textbook of Path., 1902.

HODGE: Journal of Morphology, 1892, vii. 95; 1894, ix. 1.

KLOTZ: Science, N.S., 1911, 33; 899; Jr. of Exp. Med., 1910, xii. 707; Centralblatt f. Path., 1908, xix. 537.

LEVIN AND LARKIN: Jr. of Med. Research, 1909, xxi. 319.

MACWILLIAM AND MACKIE: Jr. of Phy., 1906, xxxiv. 34-35.

STEWART, GUTHRIE, BURNS, AND PIKE: Jr. of Exp. Med., 1906, 289.

THOMA: Quoted by Adami. Inflammation, 1909, 203; also quoted in Am. Textbook of Path., 1902, 46.

WARTHIN: General Path. (Zeigler), 1908, 139.

WATTS: J. H. H. Bul., 1907, xviii. 153.

WELLS: Jr. of Med. Research, 1906, x. 149.

PART II

CHAPTER V

APPLICATIONS OF BLOOD-VESSEL SURGERY

As a result of the development of a simple and efficient method of vascular anastomoses, a wide biological field is opened to experimental investigation. But it will suffice here to give it but a rapid survey.

Morphological and microscopical study of the vascular tissues themselves has yielded information as to the power of the tissues to resist harmful influences to which they are exposed in the course of the operative procedures—namely, exposure to room temperature; mechanical manipulation; complete shutting off of the circulation in the vessel, both in the lumen and in the nutritional vessels (vasa vasorum); shutting off lymph-channels; total excision resulting in complete severance of all nervous connections; and upon the adaptive power of such tissues under altered circulatory conditions.

Notwithstanding the multiplicity of abnormal conditions under optimum circumstances, an engrafted vascular segment may not only retain its mechanical circulatory function, but its anatomical structure as well to a very high degree. It may even be called upon to perform an abnormal function, as when a segment of vein is inserted into an arterial trunk, and yet change in anatomical structure may be surprisingly moderate. As yet, these statements may only be applied to autografts, but there is some reason to hope from results obtained with other tissues that, at least in closely related individuals of the same breed, similarly perfect morphological results with isografts may be obtained.

In the case of *heterografts it is known that the anatomical* results are quite different. In fact, there may be no evidence that any of the original tissues survive, and structurally such a vascular segment may ultimately present great abnormalities—*e.g.*, fibrous thickening and calcification, together with enormous enlargement.

Yet the mechanical circulatory function may remain quite efficient. In interpreting such results, it would seem that with our present knowledge a consideration of the biolysins (or biotoxins) would be rational. From the same standpoint it is conceivable that perhaps by preliminary processes of immunization of the donor or recipient, or both, different results might be observed.

Since under certain conditions autografts may retain in a relatively high degree their normal anatomical structure, and since similar segments exposed to the action of solutions of drugs may show well-marked structural alterations, it would seem to be a promising method of comparing the toxicity of such substances and other agents.

The results attending the engrafting of preserved vascular tissues —*e.g.*, formaldehyde fixed, or tissues that have been subjected to a prolonged action of protoplasmic poisons, and which, therefore, certainly have no spark of latent vitality—are particularly of interest as regards the information yielded on the circulation of the blood, especially that an arterial blood-stream may be adequately transmitted by a dead (foreign) structure with no undesirable coagulation; the apparent replacement of the dead tissue by tissues presenting vital qualities; and the adequate vitalization of the dead tissue, with no indication that the mechanical circulatory function of the vessel is jeopardized. It may be remarked that phenomena of a similar order seem to occur in heterografted vascular segments.

In simple repair of the blood-vessels *in situ*, as when a mere opening in the wall of either an artery or vein is repaired, healing rapidly occurs; and if stenosis is not great, the histological structure of the tissues of the wall surrounding the injury apparently is not altered, barring the traumatic effects. Reunion of the ends of the divided vessels apparently results in no marked change in histological structure, excepting in the immediate vicinity of the line of union. The same seems true also when the central end of a divided vessel is united to the peripheral end of another divided vessel of similar kind and size, and the result uncomplicated by stenosis. The results of partial or complete stenosis of blood-vessels are dealt with in another place (p. 142).

If the central end of a divided artery be united to the peripheral end of a divided vein—*e.g.*, the central end of an external or internal jugular vein, or to an inferior thyroid vein—a rather well-marked, but by no means extraordinary, thickening of the wall of the vein ensues, while the arterial wall *appears* to decrease

slightly in thickness if the anastomosis and venous channels—*e.g.*, external jugular vein—permit the blood freely to escape, but sufficiently exact observations on this point are wanting; while such anastomosis to a smaller vein of a terminal character is followed by a thickening of the arterial wall with internal fibrosis and a narrowing of the arterial lumen not unlike the processes observed in simple arterial stenosis.

A fuller discussion of the vascular changes, particularly factors concerned in their production, is given under the physiological considerations (p. 103).

Observations on tissues engrafted with anastomosis of their blood-vessels are of very great biological interest. As an instance, the experiment designed for temporary results or organ perfusion may be cited.

In studying the functions of organs, a method fruitfully employed by physiologists consists in isolating the organ (*in situ*, or it may be completely removed from the body), and perfusing it through its blood-vessels with blood, or with some one of the so-called artificial blood or physiological solutions—*e.g.*, isotonic sodium chloride, Ringer's or Locke's solutions—with the view of preserving the activity of its normal functions. But owing to the rapid deterioration of tissues under such treatment, results obtained from the experiments, though yielding much valuable information, have not been altogether satisfying.*

In general it may be stated that the greatest technical difficulties have been experienced not only in procuring an adequate perfusion liquid and in its oxygenation and purification (removal of respiratory and urinary products—*i.e.*, end-products of tissue metabolism)

* Howell and Greene's Solutions.

		Per Cent.	Gm. per Litre.
I.	NaCl	0·700	7·00
	$CaCl_2$	0·026	0·26
	KCl	0·030	0·30
II.	NaCl	0·700	7·00
	$CaCl_2$	0·066	0·66
	KCl	0·040	0·40

Locke's Solutions.

		Per Cent.	Gm. per Litre.
I.	NaCl	0·900	9·000
	Dextrose	0·100	1·000
	$CaCl_2$	0·020	0·200
	KCl	0·020	0·200

II. The same solution, with the addition of 0·1 gramme of sodium bicarbonate per litre.

—but in the fulfilment of the physical conditions of the circulating medium, as suitable pressure and constant temperature of the solution.

Blood is, of course, readily obtainable, but as it is necessary to render it incoagulable either by injection or addition of anti-coagulant substances—*e.g.*, leech extract—or by defibrinating, its normal characters are not preserved. Indeed, it is said that so seemingly slight an alteration as the intermittent withdrawal, defibrination, and reintroduction of blood into the vessels of the animal from which it was withdrawn is sufficient to cause impairment of renal activity, even though the circulation remain good.

As to the artificial solutions used as substitutes for blood, as is well known even under optimum conditions, they are entirely unsatisfactory for many such purposes—*e.g.*, it is impossible to long maintain evidences of cerebral activity by perfusing the isolated mammalian brain with such a solution, the results being controlled by preservation of evidences of cerebral activity for a time in similar brains, with the same apparatus and technique, by using the animal's defibrinated blood.

This subject is of such interest that a partial abstract of a short paper by Drs. Stewart, Pike, and the writer, is given.*

Laborde is said to have perfused the isolated human brain, using the heads of decapitated criminals and the blood of dogs and oxen. In one case he connected by glass tubes the left carotid artery of the head with the corresponding carotid artery of a vigorous dog, and into the right carotid artery of the head he injected defibrinated ox blood. The perfusion was begun about eighteen minutes after decapitation. Stimulation of the Rolandic area of the cerebral cortex, which meanwhile had been laid bare, caused movements of the orbicularis palpebrarum muscle, of the eyebrows, the supra-orbital portion of the frontal muscles, and the elevators of the jaw—phenomena which persisted fifty minutes. In no case did Laborde get any return of voluntary movements.

Hayem and Barrier decapitated dogs and perfused the heads with defibrinated blood in five experiments, and entire blood in seventeen experiments, using bottles filled with blood of horses and dogs for the purpose. Their conclusions were: (1) The corneal reflex disappears before the last respiratory movement; (2) the head then becomes completely inert and the pupils dilate, with definite death; (3) resuscitation occurs when the perfusion is made

* *American Journal of Physiology*, 1906, xvii. 311.

without delay; (4) the perfusion should be done with oxygenated blood at suitable temperature and pressure, and should be sufficiently copious and prolonged; (5) resuscitation was possible only for very brief intervals under any conditions.

An idea of our observations is conveyed by the following condensed protocols of three selected experiments:

Protocol I.

Perfusion with Locke's Solution.

Small dog, young. Ether; tracheotomy; cannula for injecting warm Locke's solution in jugular vein, connected with pressure bottle; cannula for bleeding in femoral artery; 400 c.c. to 500 c.c. of blood withdrawn.

About 700 c.c. of Locke's solution injected first time; then alternate bleeding and injection of Locke's solution until 1 litre had been injected. Corneal reflex still present when injection was stopped; reflex continued for a period of a few minutes, during which no fluid was withdrawn or added.

A second period of bleeding and injection of Locke's solution followed. Corneal reflex disappeared; then great dyspnœa and deep respiration. Heart stopped in twenty-five minutes from beginning of first bleeding; fluid escaping from femoral cannula still contained a fair number of red corpuscles.

Locke's solution, even when mixed with a considerable proportion of the animal's own blood, did not maintain the corneal reflex for any considerable length of time.

Protocol II.

Perfusion with Defibrinated Blood.

Pup. Ether; blood obtained from a dog on the previous day had been defibrinated and kept on ice for twenty-four hours was used for artificial circulation through brain.

11.23 a.m.: Tied right subclavian artery and vein; artificial respiration.

11.26: Tied aorta and put cannula in central end.

11.28: Tied inferior vena cava. Put cannula into inferior vena cava toward heart, running it up into auricle; corneal reflex present.

11.39: Tied heart in auriculo-ventricular groove, omitting the

great veins, and immediately began artificial circulation from a pressure bottle with the defibrinated blood prepared. Movements like dyspnœa, although defibrinated blood is circulating freely. Tested corneal reflex repeatedly, and found it well marked. Movements of the eyes occurred; pupils contracted.

11.47: Corneal reflex very feeble in right eye; good in left eye. Spontaneous respiratory movements ceased at this time.

11.48: Corneal reflex absent in both eyes; pupils strongly contracted. Tried for light reflex several times in last few minutes, but could not be certain of its presence.

Stimulation of vago-sympathetic nerve in neck caused dilation of pupil of right eye until 12.10; of left eye until 1.22. Corneal reflex was maintained for about nine minutes.

We concluded, from a consideration of the above data: (1) That solutions of the inorganic salts of the blood are totally inadequate to sustain the activity of the brain, including the medulla oblongata, either as regards reflex or voluntary function. Even when mixed with a considerable proportion of blood, these solutions are inadequate. (2) Defibrinated blood (oxygenated), circulated by means of a pressure bottle, maintained the activity of the reflex centres, and also of the cortical motor centres for short periods up to eight or nine minutes.

Protocol III.

Perfusion of Dog's Head with Entire Blood by Vascular Anastomosis to Another Dog. (*Cf.* p. 250.)

Two dogs, one somewhat larger than the other, were etherized. Tracheotomy. The peripheral ends of the carotid arteries and internal jugular veins of the smaller dog were anastomosed to the corresponding vessels of the larger dog. The skin-flaps from the neck were then sewed together.

4.35 to 4.36·30: Decapitated small dog in lower cervical region; respiratory movements ceased; no corneal reflex because of deep anæsthesia.

4.40: Respiratory movements of nostrils and mouth of transplanted head began; rate about 35 per minute. Corneal reflex obtained; pupils at nearly maximal dilation. Respiratory movements of transplanted head soon fell to 20 per minute. The depth of anæsthesia was reduced.

4.43: Rhythmic movements of upper eyelids of perfused head

apparently a little in advance of respiratory movements, but of same rhythm.

4.46: Movement of upper eyelids less rapid than respiratory movements of perfused head; well-marked corneal reflex.

4.47: Pupils at half-maximal dilation in transplanted head. More ether given.

4.51: Tried for light reflex of perfused head; probably not present.

4.57: Piece of meat pushed well back in throat of perfused head. Reflex movement of deglutition followed.

5.02: Pupils of perfused head smaller than at last observation.

5.07: No corneal reflex in perfused head.

Summarized, the protocol shows that movements of the eyelid were observed for about nineteen minutes. Corneal reflexes were maintained for twenty-seven minutes. Respiratory movements persisted for about thirty minutes, and were sometimes synchronous in both dogs. Swallowing movements were obtained. The results indicate activity of at least some of the mid-brain and medullary centres.

Thus it is seen that such a method of perfusion presents strong evidence of adequacy for studying the function of isolated organs. It must not be forgotten, however, that such perfusions may be made without direct anastomosis of the blood-vessels, as by connecting with oiled or paraffined tubes, or by anastomosing them by invagination. But the method by anastomosis, as previously described, seems to present certain points of superiority, as practical absence of danger of coagulation or stenosis, etc.

The ultimate results of transplanting organs and tissue masses by blood-vessel anastomoses are considered in another chapter.

As a brief consideration of further evidences of the inadequacy—or, indeed, even of the toxicity—of such solutions seem at this point to be timely, the following additional experiments are given, as they appear to have an important bearing upon this question.

A comparison of the behaviour of tissues capable of exhibiting easily observable responses to stimulation in blood and in artificial liquids is very instructive. Strips of heart-tissue from a turtle's ventricle are admirable for this purpose. When placed in the animal's own defibrinated blood, or in its serum, such a strip exhibits no contractile activity other than relatively slight tone changes; but in the commonly employed saline solutions well-marked

contractions as a rule soon appear (see p. 303). The relatively slight differences in the behaviour of the various solutions seem probably to be due to the different irritating values of the solutions themselves. That the irritating (toxic) properties of the solutions are associated with their physical characters is indicated by the fact that the addition of colloidal substances—*e.g.*, boiled starch—is followed by a decreased irritating power, for a ventricular strip placed in such a solution behaves as in blood. And, further, if this solution be replaced with colloid-free salt solution, the strip responds very much as though it had been bathed in blood. The irritating property may be said to be decreased, and characteristics similar to those of blood to be conferred upon the salt solution by the colloid.

The effect of such solutions applied to tissues during the operation of engrafting has been mentioned in connection with changes in engrafted vascular tissues (p. 104). But previously it has been observed that thin slices of thyroid exposed to the action of salt solution before being engrafted did not survive so well as similar slices treated with blood-serum. The observations on blood-vessels lead to similar conclusions.

The results obtained by perfusing the kidneys for a short time *in situ* with salt solutions give well-marked evidence of injurious action. This experiment (on cats) is followed in a large percentage of cases by the development of symptoms of uræmia, and death. Histologically, kidneys of such animals are found to have undergone profound alterations (p. 238).

Summarized, the results of such experiments show that—

1. Anæmia alone is apparently much less harmful than when accompanied by perfusion of any of the commoner salt solutions.

2. The commoner salt solutions do not seem to differ greatly in toxicity.

3. Attempts thus far to devise a non-toxic solution for perfusing—*e.g.*, salt-starch solution—have not been attended with any degree of success.

4. Anæmia with perfusion of the kidneys as a rule is followed by death of the animals within a few months, the majority dying in a few weeks.

5. The causes of the differences in time of death of the animals are unknown. Individual peculiarities may be (and probably are) an important factor.

6. Metabolic disturbances, seemingly in the direction of increased protein metabolism especially, occur.

7. Decrease in urinary secretion preceding death is probably an important factor to consider in interpreting the final symptoms, which are those of uræmic-poisoning.

8. Structural changes of a hæmorrhagic and degenerative character occur in the perfused kidneys.

It is interesting to consider if, with our present knowledge, a plausible explanation of this action can be given, since it is by such theoretical considerations that at least the practical aspects of an experimental investigation are advanced and a conception of the processes at least outlined.

In the case of simple anæmia, not only do the blood-vessels contain a fluid having normal physical properties for the cells of the kidney, but they also hold a certain amount of the pabulum for the kidney, including oxygen, in an available form. Also, they are suited to receive a certain amount of the metabolites thrown out by the kidney cells into the blood—*e.g.*, carbon dioxide—retention of which in the organ is detrimental. Further, absolute hæmostasis is difficult to accomplish under the condition of the experiment, so that renal products in the nature of "hormones" may still reach the general circulation, though, of course, in decreased amounts. However this may be, it must be concluded that the factor is in favour both of the simple anæmias and of the anæmias accompanied by perfusion, for it is well known that a tissue receiving a subminimal amount of blood (subminimal being used as indicating in the first instance an amount of blood too small to preserve the ordinary manifestations of activity—*e.g.*, in cerebral anæmia, etc.—and in the second instance that the blood is too dilute to preserve such manifestations) is easier to resuscitate than if the circulation be entirely stopped, or if the perfusion be carried out with a blood-free liquid; and that after resuscitation the normality of its subsequent activities will vary indirectly with the degree and period of anæmia. (*cf.* p. 338).

It is interesting at this point to note the work of Policard, who has reported in detail the results of an investigation undertaken with the view of determining what structural changes occur outside the body in the epithelial cells of urinary tubules under the influence of sodium chloride solutions of different concentrations. He decapitated white rats, quickly removed the kidneys and cut them into very small bits, the largest being under one millimetre in thickness. Such fragments were then immersed for fifteen minutes in salt solution of known strength at a temperature of 15° C. The

tissues were then fixed in formaldehyde solution, after which they were prepared for microscopical examination. He concludes that solutions of sodium chloride of all strengths (hypotonic, isotonic, and hypertonic) change more or less the cells of the convoluted tubules.

Now, if salt solutions are examined, it is found that they all contain one or more of the inorganic salts in approximately the proportion found in the blood. Yet they are all toxic. The same is true of the one containing, in addition to more abundant blood-salts—viz., sodium, potassium, and calcium—grape-sugar, which is considered another constituent of normal blood. In certain physical characters these solutions differ greatly from the blood, or even serum—*e.g.*, they are non-colloidal. Such being the case, we might attribute at least a part of their harmful influence to this factor. To test this point, a colloidal solution was prepared by adding boiled starch to a salt solution in such proportion that the freezing-point, electrical conductivity, and viscosity were nearly identical with normal cat's blood (defibrinated). Yet it was no improvement over the plain salt solution, as judged by the result (Cat 30, p. 277). But it would be a mistake to draw conclusions from this experiment, as starch is an abnormal colloid for blood. Besides, owing to the cooling of the kidneys during their exposure made for observing the course of the injection (room temperature was 15° C.), it is not improbable that the temperature of the solution was lowered to such an extent that its viscosity was increased. A considerably higher injection pressure was required than for the other solutions, so this, too, must be taken into account. Unfortunately, no control experiment was performed to determine the effect of merely introducing some of the solution into a cat's circulation.

Unlike blood, such solutions lack not only normal physical properties, but they cannot be considered to contain an adequate pabulum, there being no evidence that grape-sugar, which is a constituent of Locke's solution, is adequate in this direction, although it is destroyed by active tissues. Locke and Rosenheim, using surviving hearts, observed a more rapid disappearance of dextrose from the perfusion fluid during activity. McGuigan, working in my laboratory, obtained the same result for skeletal muscle prior to the appearance of Locke and Rosenheim's announcement (see p. 304). So long as the isolated skeletal muscles survive (as indicated by response to electrical stimulation), the sugar disappears. Later, the perfusion fluid filters through the walls of the blood-vessels into

the tissues, but the sugar contained therein does not appear to be destroyed. Still, since the period of anæmia is relatively short, and since organs, or even cells, like animals, undoubtedly contain a certain amount of material that for a time can take the place of that supplied by the blood, too much stress should not be laid on this point. Even a certain store of oxygen is laid up in the tissues themselves that can be drawn on in such emergency conditions, but there is no evidence that the kidney has a sufficient store to last any great length of time, as is the case in muscle.

Although the solutions employed in perfusing the kidneys were well aerated, they contained but a fraction of the amount of oxygen found in arterial blood—indeed, the amount even under pure oxygen is insignificant compared with ordinary venous blood. So it may be concluded that the tissues received too little oxygen. Again, the carrying capacity for carbon dioxide of such solutions is far less than that of blood; also, the total amount of solution injected into kidneys, compared to the amount of blood passing through them normally in the same length of time, is insignificant. We may conclude, therefore, that in anæmia with perfusion, as well as in anæmia alone, there is a profound disturbance of renal respiration, and that this is probably greater in the former than in the latter case. Although some blood probably entered the renal vessels and became mixed with the perfusion solution, the total amount thus entering, considering all other factors as being the same, would be less during perfusion, owing to the greater pressure of the perfusion liquid; also, such as entered the vessels and became mixed with the solution probably had a less metabolic value per unit, owing to the dilution. Numerous other possibilities might be brought forward, but what is written above is sufficient to indicate the state and complexity of the problem.

In the case of transplantation of tissue masses or organs with anastomosis of the blood-vessels, the facts presented regarding the toxicity of salt solution shed much light on the results, which have thus far in general been imperfect. But, as has been pointed out elsewhere (p. 196), under certain conditions we may hope for more satisfactory results when such operations are performed without perfusion of the blood-vessels with salt solutions, or, indeed, even without interruption of the circulation (p. 204). If this be realized, much information may thus be obtained, not only upon the functions and inter-relationships of different organs, but upon questions of heredity as well (p. 195).

By anastomosis of the blood-vessels of an isolated preparation with suitable blood-vessels of a closely related animal a liquid of optimum character (living, undefibrinated blood) may be employed, and optimum mechanical conditions for perfusion of isolated organs or tissue masses may be fulfilled. The superiority of this method of perfusion in certain respects is demonstrated by thus perfusing the brain, since preservation of evidences of activity of the lower cerebral centres indicates the fulfilment of the nutritional conditions in a high degree.

A method of uniting the vessels by suture for the purpose of perfusion, as practised above, approaches the ideal more nearly than any other method we have at present. By such a method the factor of coagulation at the point of junction of the two vessels, which usually occurs sooner or later when cannulæ are used, is eliminated. Such procedure, however, is not always possible, for it is sometimes desirable to make an anastomosis in a shorter period of time than that required for suturing the blood-vessels. In such an experiment as transplanting the head where a double blood supply—two carotid arteries—is available, the anastomoses may be made without subjecting the engrafted head to any period of complete anæmia, for the vessels of one side may be anastomosed while the head to be engrafted is still receiving its own blood-supply. The factor of anæmia especially, introduces undesirable conditions when the perfusion is done for the purpose of studying the action of drugs upon the nervous tissues, for such tissues are highly susceptible to the injurious influences of anæmia. Recourse must then be had to other methods of re-establishing the vascular communication, which can be done in a shorter period of time. The most commonly employed method is the use of cannulæ. Although the walls of such cannulæ may be coated with oil or paraffin, coagulation usually sets in early. In such perfusion studies, therefore, it has usually been found advisable to make use of some coagulation retarding agent, such as peptone or leech extract. I have even obtained good results without the use of any such agents by employing short hour-glass-shaped, paraffin-coated cannulæ. Such anastomoses as I have practised were made between the common carotid artery and abdominal aorta, and the external jugular vein and inferior vena cava of dogs and cats. In such a procedure it is necessary to isolate as much of the vessels as is necessary to make the connection.

By such perfusion it is possible to study the physiological activity

of different parts of the body under different conditions. Such methods are especially valuable in studying the actions of drugs upon the integral elements of such a complex unit as the central nervous system. For example, Gaskell and Shore studied the action of chloroform upon the brain by joining the central ends of the common carotid arteries and external jugular veins of one animal to the peripheral ends of similar vessels in another animal. Thus, in one animal the brain and spinal cord were supplied by separate and distinct circulations. Then, by administering chloroform to the animal whose blood supplied the head of the other animal—the feeder—the effect of this drug on the brain alone could be studied.

Ryan and McGuigan have made use of a method of transfusion in studying the site of action of strychnine in the spinal cord. Their idea was to poison a limited region of the spinal cord with strychnine under normal circulatory conditions. In virtue of the anatomical connections of the cord elements, they were able to show that the irritability of the sensory or intermediate cells of the spinal cord was increased in mammals by strychnine. This was based on the observation that in such a condition of local poisoning spasms could be obtained in the unpoisoned region of the animal through stimulating the skin in the poisoned region. As illustrative of such transfusion methods, a brief statement of their technique and methods of study will be given.

Two animals were selected in the weight ratio of two and a half or three to one. Tracheal cannulæ were inserted. In the larger animal, or donor, a cannula was first inserted into the femoral vein, and was connected to a burette preparatory for the subsequent injection of peptone, which, however, was not injected until the dissection in the donor was complete. The two carotid arteries and one external jugular vein were isolated, and cannulæ inserted. With Y-tube connections the two carotid arteries were made to have a single outlet, which was to be connected with the thoracic aorta of the recipient. A rubber connection was also placed upon the cannula in the external jugular vein, which was to be connected to the inferior vena cava. All cannulæ and rubber connections were previously coated with a thin layer of paraffin. When the dissection was completed, an injection of 10 per cent. peptone in 0·9 per cent. sodium chloride solution was begun. The dose usually given was 0·25 gramme per kilo.

In the smaller animal—the recipient—the thorax was opened by

removing six or seven ribs on one side. Artificial respiration was given. Through the window in the chest wall the inferior vena cava and thoracic aorta were isolated. The vena azygos major and thoracic duct were ligated to prevent a subsequent spread of the strychnine from the lower to the upper parts of the animal.

Cannulæ were inserted into the peripheral ends of the thoracic aorta and the inferior vena cava. Connections were then made between the carotid artery of the donor and peripheral end of the thoracic aorta of the recipient, and the external jugular vein of the donor and inferior vena cava of the recipient. The period of anæmia could be reduced to two and a half minutes in making the connections. After the perfusion was begun, the pulse was strong in the posterior extremities of the recipient, the return circulation was excellent, and when the ball of the foot was incised it bled freely.

After the injection of appropriate doses of strychnine into the tubes between the donor and recipient, thereby poisoning the lower half of the recipient, spasms were first obtained in the lower region alone when cutaneous stimulation was applied in this region. In a short time stimulation of the skin in the poisoned region gave general spasms, while stimulation of the skin in the unpoisoned region gave only ordinary or no response. Spontaneous general spasms then ensued. At this period the spinal cord was severed at the level of the anastomosis. Spasms then continued in the lower half of the animal, but ceased above. Stimulation of the skin in the upper portion of the animal then gave only normal response, while stimulation below gave spasms confined to the lower half. Strychnine was immediately injected into the upper half of the animal, and was followed by typical strychnine spasms in the upper half. These observations showed that at the time of the initial strychnine-poisoning of the lower half of the animal, with manifestations of general spasms, the spasms of the upper part of the animal, when this region was unpoisoned, were due to influences which reached the motor cells from poisoned sensory cells, thus showing that the irritability of the sensory cells was increased by strychnine.

Many applications have been made of the method of transfusion in the study of biological processes, and as yet there remains a wide unexplored field.

Practicability of Operations upon Blood-Vessels.

Abundance of proof is at hand to show that suture, repair, and anastomosis of blood-vessels, from the experimental standpoint, is not only feasible, but relatively easy of successful execution under the conditions described.

Surgically, all the operations so tested have been entirely successful in both efficiency and permanency of function. In addition to the evidence obtained by clinical examination, such as good pulse, etc., and by direct examination of the tissues, such as very perfect union with smooth intimal covering and absence of stenosis, efficiency of vascular anastomosis was strikingly demonstrated. Twenty days after division and restoration of one common carotid artery, another dog's head was engrafted on to the neck by dividing the operated common carotid artery peripherally to the line of the anastomosis, and anastomosing the central end to the peripheral end of one carotid artery of the engrafted head. After anastomosis of the external jugular veins, the circulation was turned into the engrafted head, and, notwithstanding the fact that the blood had to pass through both the old and new anastomoses, the circulation was sufficiently adequate to bring about resuscitation in the engrafted head, with apparently a full return of consciousness, and to maintain it for several hours, or until chloroform was administered. Again, the results which Carrel and the writer have reported conjointly and individually, and the results of Watts and others, place the question of efficiency beyond doubt.

Permanency has been demonstrated in a large number of animals, and for different operations. For example, one of my dogs had a reversed circulation of arterial blood in one of the external jugular veins for more than five years; another dog, also in excellent condition, presents an active circulation through a carotid artery into which a segment of formaldehyde-fixed vena cava of another dog was engrafted more than three years ago. Again, a carotid artery of another dog, repaired in a similar manner with a segment of aorta from a rabbit, was functionating splendidly when the animal was chloroformed some seven months after the operation. Permanency of results in Eck's fistula in cats also has been mentioned (p. 101). Permanency, therefore, appears to follow all such successful vascular anastomoses, notwithstanding the occurrence in certain cases of profound anatomical alterations of the engrafted portion of the vessel.

Practicability is another important consideration from this (the surgeon's) standpoint. The simplicity of the operative procedures has been sufficiently dwelt upon elsewhere (p. 81).

All successful investigators in the field of vascular surgery have emphasized the importance of aseptic technique, and, of course, this should be followed in all vascular operations as in any other surgical operation. But emphasis upon this principle, from the standpoint of successful vascular suture alone, has been unduly insisted upon. For there is a mass of experimental evidence proving conclusively that blood-vessels may be not only repaired, but that the more extensive operations of end-to-end union of divided blood-vessels may be successfully accomplished with a non-rigidly aseptic technique. It is quite as essential for success to exactly carry out the mechanical features of the technique, especially as regards the accurate approximation of the intimal surfaces, and the infliction of minimal trauma. And for this there are good theoretical explanations. For example, owing to the flow of blood through the lumen of the vessel past the point of suture, and escape of blood outward from the vessel through the unavoidable suture trauma, any substances introduced into the wall of the vessel or into the lumen, if not too firmly attached, would be carried away. Also, owing to the well-known bactericidal action of the blood, both by phagocytosis and bacteriolysis, it tends to destroy any bacteria with which it may come in contact. And as such action presumably varies directly according to the quantity of blood coming in contact with the bacteria, it seems clear that such bactericidal action would be greater in the blood-vessels than in the tissues and spaces outside the blood-vessels. Furthermore, it is a well-established fact that the tissues of the blood-vessels are relatively resistant to suppurative influences. In witness of this may be quoted the well-known observations that in pulmonary tuberculosis blood-vessels may extend across cavities, resulting from necrosis of the lung-tissue with pyæmic infection and abscess formation, and adequately transmit the blood without leakage. Even the highly resistant tissues of the lung in this instance break down and disappear, leaving the tissues of the walls of the blood-vessels insufficiently damaged to cause rupture, although the supporting perivascular structures are absent.

Experiments published by Dorrance in 1906 show that surgical uncleanliness does not necessarily prohibit successful vascular suture. He employed a method similar to that described by

Clermont in 1901, which consisted essentially of the union of the vascular edges by means of a continuous suture of fine thread. Of a total of fourteen operations, twelve suppurated. Three of the operations were complete circular sutures. The specimens were examined from two to forty-two days after the operations. In two cases there was complete thrombosis, in five there were small thrombi, while in seven no visible thrombi were present.

The ease with which operative proficiency is achieved is one of the most pleasing features of the experiments; indeed, the ordinarily skilful surgeon readily masters it during his first operation. The manipulations appear to be vastly more difficult to the onlooker than they are in reality.

Of course, some means of producing temporary hæmostasis without much injury to the vessels is essential. The method by the use of ordinary serrefines or bull-dog forceps (p. 31) is recommended, but many other efficient and safe methods will occur to the surgeon. As previously described a simple method of compression with a coarse ligature or narrow strip of cloth used as a snare, with a short rigid tube to draw it through to hold it, and forceps, or with forceps alone to tighten and hold it, is always available during an operation, and may be confidently resorted to, as when suitable special forceps or other instruments for temporary vascular occlusion are not at hand. In fact, this method of compression has a number of good points in its favour that will readily occur to the surgeon.

For large to medium vessels (say down to those having a diameter of about four millimetres), No. 12 cambric needles (which may be obtained at any dry-goods store) will do, though for the smaller vessels smaller needles are better. For very small vessels, the smaller needles (Nos. 14 to 16) are necessary for the best results.

The suture material may be either hair (human hair is excellent) or very fine-fibred thread, such as silk. Ordinary sewing-silk is rather too coarse, but the finest and best grades of such thread may be employed by splitting before threading into the needles. A full account of the preparation of such needles and thread is given on page 24.

A ready source of material for repairing blood-vessels—as when segments are missing, or if for other reasons e.g., retraction, it is desirable or necessary to lengthen the vascular tube—is the animal upon which the operation is to be performed. For example, on

the dog it is a simple and safe procedure to remove a suitable segment from an external jugular vein to restore the continuity of a divided common carotid artery; or a suitable vascular segment may be taken from another species. At least, all such heterotransplantations thus far reported have given positive evidence of their efficiency; indeed, even when segments of blood-vessels are taken from cold-storage tissues, they may adequately serve such purposes (p. 10). But since there is no evidence that such tissues survive, and putrefaction and other processes—*e.g.*, autolytic—may occur in such tissues, thereby introducing the possibility of very grave complications—*e.g.*, blood-poisoning—if utilized for repairing blood-vessels; and since formaldehyde-fixed vessels serve the purpose, and are not open to the objection cited in the case of cold-storage vessels; and since there is no evidence that a cold-storage vessel can functionate superiorly to a formaldehyde-fixed one, I consider the use of cold-storage vascular tissues unwarrantable, excepting, perhaps, under very exceptionable conditions.

Perfectly fresh tissue from the same, or another individual of the same species, is recommended whenever convenient, as the maximum preservation of anatomical structure will be assured, particularly in the case of the autograft, and the mechanical factors for a perfect operation will be optimum. A fresh heterograft, or tissue taken from an animal of a different species, will fulfil the mechanical conditions quite satisfactorily, both as to operative manipulation and mechanical circulatory function. The formaldehyde-treated tissues will meet the operative conditions less perfectly, but success with such may be achieved without great difficulty, and the mechanical circulatory function has been quite satisfactory in our hands. From the results hitherto achieved it even seems possible that tissues not of animal origin might be successfully employed, but this must be established experimentally. So the operator has access to a wide assortment of reliable material.

It may be added that since such tissues are so readily obtainable, as at a slaughter-house, it would seem to be a practicable plan to fix and prepare a suitable supply for emergency use.

Results are, of course, the most important consideration. Since they have in large part been indicated above, it will suffice to say in conclusion that in my experiments *not one clinical symptom attributable to an operation solely upon a blood-vessel* has been observed to contra-indicate similar operations on similar animals for therapeutic purposes.

REFERENCES.

CLERMONT: Presse Médicale, 1901.

CRISTIANI: C. R. de la S. de B., 1904, 192, 194, 225; *ibid.*, lvi. 1905, lvii. 68, 531, 754; Jr. de Physiol. et de Path. Générale, 1905, vii. 261.

CROWE, CUSHING, AND HOMANS: J. H. H. Bul., 1910, xx. 127.

DORRANCE: Annals of Surg., 1906, xliv. 409.

GASKILL AND SHORE: B. M. J., 1893, 105, 164, 222.

GREENE: Am. Jr. of Phy., 1898, ii. 82.

GUTHRIE: Am. Jr. of Phy., 1903, viii. 441; *ibid.*, 1907, xix. 482; Jr. of the Am. Med. Assoc., 1908, li. 1658; Jr. of Exp. Zoology, 1908, v. 563; also Am. Jr. of Phy., 1907, xix. 16; Archiv. Internationales de Physiologie, 1907, v. 108; Wash. Univ. Bul., 1908, vii. [illegible]; Jr. of the Am. Med. Assoc., 1909, li. 1314; Wash. Univ. Bul., 1907, 165; Proc. of the Soc. for Exp. Biol. and Med., 1910, vii. 26, 27, 95; Science, N.S., 1908, xxvii. 473; Ar. of In. Med., 1910, v. 232; Heart, 1910, ii. 115; Jr. of the Am. Med. Assoc., 1910, liv. 831; *ibid.*, 1908, l. 1035.

GUTHRIE, F. V., AND C. C.: Jr. of the Am. Med. Assoc., 1910, liv. 349.

GUTHRIE AND PIKE: Science, N.S., 1906, xxiv. 52; Am. Jr. of Phy., 1907, xviii. 14.

GUTHRIE, PIKE, AND STEWART: Am. Jr. of Phy., 1906-07, xvii. 344.

HAYEM AND BARRIER: Archiv. de Physiol., 1887, x. 1.

HILL: The Physiology and Pathology of the Cerebral Circulation, London, 1896.

HOWELL: Am. Jr. of Phy., 1902, vi. 181.

LABORDE: Cited by Hayem and Barrier.

LOCKE: Centralblatt f. Physiol., 1901, xiv. 670, 672.

LOCKE AND ROSENHEIM: Jr. of Phy., 1907, xxxvi. 205.

MCGUIGAN: Am. Jr. of Phy., 1908, xxi. 334.

PIKE, GUTHRIE, AND STEWART: Jr. of Exp. Med., 1908, x. 371, 490; Am. Jr. of Phy., 1908, xxi. 359; *ibid.*, 1908, xxii. 51.

RYAN AND MCGUIGAN: Jr. of Exp. Pharmacology and Therapeutics, 1911.

SOLLMANN: Am. Jr. of Phy., 1905-06, xv. 121.

STEWART, GUTHRIE, AND PIKE: Jr. of Exp. Med., 1906, viii. 289.

POLICARD: Jr. de Physiol. et Path. Générale, 1908, x. 249.

Results of Replantation of the Thigh.

The operation was performed on about an 8-kilogramme white dog, under ether. Circular incision of the skin was made immediately below the knee and the internal saphenous vein ligated. A

second incision, perpendicular and continuous to the first one, was made along the femoral vessels as far as the upper part of Scarpa's triangle. The skin about the circular incision was dissected and retracted upward as far as the lower part of the thigh. The edges of the skin on either side of the longitudinal incision were dissected for about ½ inch, the femoral aponeurosis exposed and opened, and the femoral vessels and nerve dissected and severed at the middle portion of the thigh. Section of the sartorius and femoral quadriceps was made about 3 centimetres above the knee. Also section of the sciatic nerve and of the biceps, semitendinosus, internus rectus, adductor longus, and semimembranosus muscles, was performed at different levels. Afterward the femur was cut at the union of its lower and middle thirds. The limb was then removed and enveloped with sterilized moist compresses.

After a few minutes the amputated portion of the limb was placed on the operating table close to the remaining stump of the thigh.

The continuity of the artery and vein was immediately re-established by end-to-end suture. The two ends of the bone were closely approximated and sutured together with silver wire.

The temporary hæmostatic clamps were then removed and the circulation immediately restored through the peripheral parts of the artery and veins. Absolutely no blood escaped from the vessels at the lines of anastomoses. The pulsations of the popliteal artery immediately became normal, and the femoral vein filled with circulating venous-hued blood. The peripheral end of the cut muscles began to bleed slowly.

The cut ends of the sciatic nerve were then sutured together with silk, and the muscles, aponeurosis, and skin with catgut. The line of cutaneous sutures was covered by a dressing of gauze and collodion. Afterward the lower portion of the abdomen, hip, thigh, and leg were enveloped with cotton and a large plaster of Paris bandage.

Before putting on the dressing the state of the circulation in the limb was examined. The pulsations of the popliteal and posterior tibial arteries were as strong as the pulsations of the same arteries in the other limb. In hue, the replanted foot was a little redder, and the temperature to the touch a little higher than was the temperature of the other foot and leg. The vaso-dilation was similar to that observed following the use of an Esmarch bandage.

There were no dead spaces between the tissues, excepting a small one near the bone. The hue of the peripheral end of the muscles was darker than that of the central end. The connective tissue of the thigh and of the popliteal region seemed normal, while in the leg and foot below the ring of constriction it was markedly infiltrated and œdematous. The veins of the foot and leg were extremely dilated and filled with coagulated blood. The circular constriction produced by the gauze collodion dressing had stopped the venous circulation, as it sometimes happens in human surgery when a dressing is too tightly applied—*e.g.*, in the dressing of fractures. At first there may be a feeble circulation through the constricted veins, but this soon stops and the limb becomes swollen. Shortly after the arterial circulation also stops and gangrene develops.

Summarized, this experiment shows that the circulation may be easily and entirely re-established through a replanted thigh. The pulsations of the femoral, popliteal and posterior tibial arteries were as strong as the pulsations of the corresponding arteries of the other side. The arterial circulation seemingly was normal.

The capillary circulation was exaggerated, the temperature of the limb being higher and its hue redder, owing, doubtless, to the fact that the vasomotor nerves were cut.

The venous circulation was observed to be good immediately after the operation; but the post-mortem examination demonstrated that between the point of compression by the circular dressing and the anastomoses of the vessels there was neither infiltration nor œdema of the connective tissue. The hue of the muscles peripheral to the line of amputation, however, was darker than the hue of the muscles central to the line. This difference was probably due to venous congestion.

The greatest departure from normal observed in the character of the circulation of the replanted limb was dilation of the smaller vessels. It is improbable that this vaso-dilation of itself would have produced serious swelling of the limb. Doubtless the replanted limb increased in size owing to the vaso-dilation, and this would have, of course, increased the tightness of the bandage. Examination of a transplanted kidney and of a replanted thyroid gland showed both to be enlarged in size, owing probably to the increase in the circulation.*

* The above experiment is quoted from a paper by Carrel and the writer in the *American Journal of the Medical Sciences*, February, 1906.

A similar experiment, extending over a longer post-operative period, gave the following results:

The animal employed was a small white bitch. Through a longitudinal incision the vessels of the thigh were exposed and cut above the point of Scarpa's triangle. The skin was circularly severed and the thigh completely amputated above the junction of its lower and middle third. After a few minutes the limb was replanted. The ends of the bone, the muscles, the vessels, and the sciatic nerve, were united. The circulation was re-established after having been interrupted for one and a quarter hours. The pulsations of the popliteal and saphenous arteries were normal. The venous-hued blood circulated very actively through the femoral and saphenous veins. Arterial-hued blood flowed from the small arteries of the peripheral part of the limb. The skin was sutured and a plaster dressing applied to the limb and trunk.

After the operation the general and local conditions of the animal remained very satisfactory. It drank and ate normally and walked on its three sound limbs. The skin of the replanted foot remained normal, but its hue was redder and its temperature higher than that of the normal foot. The anterior part of the foot soon became moderately swollen.

Seven days after the operation the dressing was partially removed. The limb presented neither œdema nor trophic troubles. The œdema of the anterior part of the foot was doubtless due to pressure by the lower edge of the bandage, as the swelling completely disappeared within a few hours after correcting the fault of the dressing. The skin was normal and the wound was uniting, *per primam intentionem*, without evidence of inflammation. The temperature of the skin was higher below than above the line of suturing.

Eight days after the operation the foot appeared normal in size, all œdema having disappeared.

On the tenth day, during the afternoon, the temperature of the replanted foot became lower—*i.e.*, similar to that of the normal foot. The dressing was then removed. It was found that, owing to a slipping of the plaster bandage, some urine had got into the cotton dressing and caused infection of the upper part of the longitudinal incision. A small subcutaneous abscess had developed along the vessels. The general conditions of the animal were excellent, and the nutrition of the limb satisfactory. As the arterial pulsations were much weakened, and as it was considered important to accurately determine the cause of this change, the

animal was etherized and the vessels examined through cutaneous incisions, after which it was killed.

This dissection *in vivo* under ether gave the following results: The point of the vascular anastomosis was surrounded by the small subcutaneous abscess. The venous anastomosis was good. The arterial anastomosis was partially occluded by a small clot. All the other portions of the vessels appeared perfectly normal. The circulation through the limb was yet satisfactory, as the obliteration of the anastomosis was not complete. The union of the skin, the muscles, and the sciatic nerve, was normal. The process of the consolida-

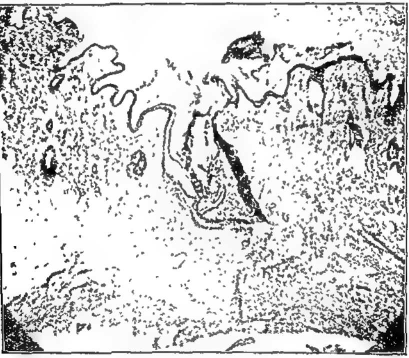


FIG. 103.—REUNION OF SKIN OF AUTO-ENGRAFTED LEG AND STUMP AFTER ELEVEN DAYS (DOG).

tion of the bone was beginning. It is possible, but not certain, that, if the animal had been allowed to live, the arterial stenosis would have gradually increased, and that in the end the circulation would have been interrupted. Then no doubt gangrene of the limb would have occurred, which result would have been due primarily to the secondary infection.

Therefore, the circulation of a replanted limb, re-established an hour and a quarter after interruption, by end-to-end anastomosis of the femoral artery and vein, was adequate, as judged by the metabolism of the limb.

No trophic trouble occurred during ten days. Healing of the severed tissues appeared to be as rapid and complete, as after an ordinary surgical wound.*

Result of Transplantation of the Fore-Leg.

May 14, 1908.—Large brown male spaniel. The right fore-leg was removed at the shoulder and replaced by a leg from another animal. The operation was completed at 5.45 p.m. The animal came out from the ether with only a slight amount of nausea. The pulse in the transplanted leg was good and the foot was warm. Soon learned to care for the foot. Seemed to be in no pain. Had several naps, between which it would move about, drink water, etc.

May 15, 1908.—Foot gradually becoming swollen; pulse good and foot warm. Opened dressing at 1 p.m.; wound looks good; cut two or three stitches; dressed with boric acid.

May 16, 1908.—Size and condition of foot about the same. Ate, and urinated freely. Changed dressing about five o'clock.

May 17, 1908.—Dog in fine condition; apparently no change; foot warm; in no pain.

May 18, 1908.—Condition about the same as before; wound in good shape; serous fluid pressed from inner part of wound; cleaned wound with hydrogen peroxide, and dressed with boric acid. Leg pink and warmer than unoperated leg. Dog ate well and urinated freely.

May 19, 1908.—Dog in fine condition. Dressing moist; removed dressing. Entire leg and shoulder is somewhat larger. Sponged with bichloride of mercury solution and dressed with iodoform.

Later, owing to suppuration, the dog was chloroformed, but the records have been misplaced.

Results of Transplantation of Kidneys.

Only transplantation of renal tissue with anastomosis of blood-vessels will be considered, since a very important function of the kidney is well known to be the separation from the blood and of excretion of waste products, retention of which is rapidly detrimental or fatal to the animal. Obviously, then, to approach anywhere near to the normal conditions of such an organ it is necessary

* The above experiment is quoted from a paper by Carrel and the writer in *Science*, N.S., vol. xxiii., No. 584, pp. 393-394, March 9, 1906.

to provide a functional as well as a nutrient blood-supply, and to provide a channel for the escape of the excretions to the outside of the body; otherwise a functional test of the operation is impossible. Also, this is necessary not only for anatomical reasons (connections of tubules, etc.), but an animal cannot long survive mere excision of renal tissue in excess of three-fourths of the total amount; for, in spite of a polyuria, a fatal derangement of metabolism is said to follow. That the protein metabolism is particularly affected is indicated by the rapid wasting of the muscular tissues and large amounts of urea excreted.*

This upsetting of the metabolism has been attributed by Bradford to lack of internal renal secretion. It would seem from this standpoint that the internal secretion of less than one-half of one kidney is insufficient to maintain life. It is necessary, therefore, to engraft one-half or more of a kidney, fulfilling at the same time the requirements as to a functional circulation and to an excretory channel. A mass of tissue of this size could not possibly survive without attention to the blood-vessels, at least in any but very small animals, even if there were no other valid reason against employment of the simple method. Since it is well known that one kidney is adequate for maintaining life, and since the entire kidney is easiest to handle, such operations should be performed with the entire organ, or both.

Floresco seems to have been the first to publish a feasible method of transplanting the entire kidney with anastomosis of the blood-vessels and report successful results. He used dogs.

The kidneys transplanted by Floresco were not, so far as I am aware, successfully put to the functional test—*i.e.*, not all of the original kidney tissue was removed, and therefore his results are not conclusive.

Floresco first tried to engraft a kidney into the inguinal region, using the femoral artery and vein for anastomosis with the renal artery and vein. Such kidneys, he said, retained vitality for a day, at which time necrosis set in, which lasted from forty-eight to ninety-five hours longer. The failure of the operation was attributed principally to the unfavourable site. Next he engrafted the kidney into the cervical region, using the carotid artery and jugular vein for anastomosis with the renal vessels. In such experiments secretion of urine was observed for a week. Owing to infection and necrosis of the ureter the observations were discontinued

* *Cf.* Stewart, "Manual of Physiology," 1910, 569.

on the tenth day. The unsatisfactory result was attributed to the abnormal location of the kidney.

He next engrafted into the abdominal region. The operation was performed by removing the kidney from one dog, the host, and replacing it with the kidney from another dog by anastomosing the renal artery and veins. The ureter was made to open on the skin. Necrosis occurred in from twenty-four to seventy-two hours.

He then considered the influences of length of operation, and concluded that an hour was too long a time. Also, he compared various methods of treatment during the operation. He tried displacing blood from the kidney with 0·75 to 1·0 per cent. salt solution, and with Locke's solution. He concluded that the use of liquids to remove the blood, the liquids being of a character designed to preserve the vitality of the tissues, did not render the operation permanently successful. He considered that the necrosis observed in kidneys transplanted without perfusion was due to the intravascular coagulation. But when coagulation was prevented by perfusion with a non-coagulable liquid, the results were not much different (*cf.* p. 236).

He then tried rendering the blood incoagulable by peptone and leech extract injections. Again, he was unsuccessful in obtaining permanent results. But in the experiment in which peptone was injected, and the ureter anastomosed to the ureter, and the normal kidney removed, the animal was alive and in good condition after eight days. His longest result is shown in the following protocol:

Experiment III.—Ureter anastomosed to another ureter. Two dogs are anæsthetized with ether. The kidney of one is removed by the dorsal lumbar way; it is small. The renal vessels are dissected for a considerable distance. Urine flows through the ureter in large quantities.

The kidney of the second dog is raised up and dissected. (The urine of the dog had been analyzed before the operation.) The end of the renal artery of the first kidney is very near to the bifurcation. By means of forceps one spreads the end of the artery. Anastomosis of the vessels is made very rapidly and very easily. (The operation lasted half an hour.) On removing the forceps, the arterial flow is re-established by the superior branch of the bifurcation, which is very near the level of the anastomosis. The anastomosed vein does not present any oozing of blood. The ureter, by the orifice whence one sees the flow of urine, is anastomosed to the peripheral end of the second ureter.

In addition to what was done in the preceding experiment, the nerve of the first kidney was anastomosed to the central end of the nerve of the second kidney.

The wound washed with sterile water was closed by a three-plane suture.

Second Day.—Animal drinks water. . . . No increase in temperature.

Third Day.—The animal in good condition; eats meat. . . . No fever. The urine is a little hard to collect; it does not differ from that before the operation.

Fourth Day.—Animal, which is well supported, drinks milk ravenously. The dog is gay.

Fifth Day.—The wound presents only two points of suture not healed. Animal eats meat; runs in yard.

Tenth Day.—Dog in good condition; eats meat; thirsty; no fever. Wound not healed on ventral side for distance of 1 centimetre.

Fifteenth Day.—Animal is well (cured); eats well; urine clear. Comes when called, and allows petting.

Sixteenth Day.—Dog again anæsthetized; opened old wound for a short distance. Through the opening one observes the transplanted kidney. No portion is flabby, and after a short observation of the kidney the wound is washed and carefully closed.

Second Day (seventeen days after the first operation).—The animal drinks and eats well; the wound does not present suppuration; the dog is running in the yard.

Sixth Day (twenty-one days after the first operation).—Almost healed.

Tenth Day.—Same condition.

In this dog the right kidney was later removed.

Floresco concluded that—

1. Transplantation of kidney is very difficult, but possible.

2. Failure of the transplantation of kidney due to site and stasis of blood-vessels.

The abdominal region is the only place favourable for survival of the kidney. The depth of the organ, situation, protection by muscles, and surrounding organs and renal pressure, important factors. Such conditions found constant only here. Not present in cervical region nor inguinal region. Failure, perhaps, also due to stasis of blood, which determines necrosis of the kidney.

3. Blood stasis cannot be dispelled by the liquids which provide a

prolonged vitality of the kidney and which prevent coagulation, or are able to destroy stasis of blood. Vaseline alone, which forms a fatty coat, prevents stasis, which is the true cause which determines renal necrosis and unsuccessful transplantation of the kidney.

4. The proceedings of anastomosis termino-terminal or by imbrication are the only two good methods. (He prefers the former, which is very simple and rapid, but uses four threads, which prevents constriction of the vessel.)

A kidney which presents a bifurcated renal artery ought to be abandoned (ordinarily, of ten kidneys, there is one that presents bifurcation near the hilum). . . .

5. The nerve of the transplanted kidney is anastomosed to the end of the renal nerve of the dog upon which the transplantation is made.

6. Action of liquids, which prevent the coagulation of blood and increases the resistance of the kidney, may have a favourable influence on the transplantation of the kidney.

7. The ureter must not be fastened to the skin, as this is always a cause of infection, which determines sooner or later the death of the animal. The ureter ought to be anastomosed to the peripheral end of the ureter of the dog. The anastomosis of two ends of the ureter may start necrosis of the ureter, which may extend up to the kidney and produce death. Anastomosis of two ureteral ends ought to be made by two planes : interior and exterior.

8. The survival of a dog with a transplanted kidney has been in one case of twelve days ; in another case, where on one side is a transplanted kidney, and on the other a normal kidney, the dog is well even after a month.

Later, in 1905, Carrel and I engrafted a kidney into the cervical region in a manner similar to that practised by Ullmann (p. 13), with excellent temporary results as regards the circulation and preservation of excretory function.

The kidney of a small dog was extirpated and transplanted into the neck. The renal artery was united to the carotid artery, the renal vein to the external jugular vein, and the ureter to the oesophagus. Three days after the operation the neck and the abdomen were opened in order to study the functions of the transplanted kidney, and to compare them with the functions of the normal kidney. The transplanted kidney was found adherent to the muscles, and dissection was necessary to free it. In size it was

larger than the normal kidney. Its hue was darker. To the touch the consistency of its tissue was normal, and the pulsations of its tissue were normal, and the pulsations of its artery were as strong as the pulsations of the artery of the normal kidney.

The circulation of the transplanted kidney was slightly greater than in the normal kidney, as detected by the touch, copiousness of hæmorrhage from incision in cortex, and pulse tracings.

The secretion of urine by the transplanted kidney was about five times more rapid than by the normal one. The intravenous injection of sodium chloride solution caused no change in the rate of the secretion in the normal, but markedly increased the rate of the secretion in the transplanted organ.

The composition of urine secreted by the transplanted kidney differed somewhat from that secreted by the normal one. The constituents were similar, but the chlorides appeared to be more abundant in the urine from the transplanted kidney, while the organic sulphates, pigments, and urea were more abundant in the urine from the normal organ.*

After having devised a method of transplanting tissues in mass —*i.e.*, with their surrounding structures—obtaining an adequate blood-supply by using the parent blood-vessels—*e.g.*, in the case of the kidneys—interposing segments of the aorta bearing the renal vessels between the cut ends of the corresponding vessels of the host, we practised renal iso-transplantation on dogs and cats with excellent temporary results.

Result of Transplantation of Both Kidneys from a Dog into a Bitch, with Removal of Both Normal Kidneys from the Latter.

A large-sized terrier was anæsthetized, and both kidneys and the upper part of the ureters were removed, together with their vessels, nerves, nervous ganglia, the surrounding connective tissue, the suprarenal glands, the peritoneum, and the corresponding segments of the aorta and vena cava. The mass was then placed in a vessel of isotonic sodium chloride solution, and the dog killed.

A small young bitch was then anæsthetized, and the abdomen opened through a half-circular transverse laparotomy. The aorta and vena cava were cut a little above the mouth of the ovarian vessels. The kidneys of the dog were then removed from the salt solution, and put into the abdominal cavity of the bitch, and the

* The above experiment is quoted from a paper by Carrel and the writer in *Science*, N.S., vol. xxii., No. 563, p. 473, October 13, 1905.

segments of the aorta and vena cava were interposed by biterminal anastomosis between the cut ends of the aorta and vena cava of the bitch. The circulation was re-established, after having been interrupted for one hour and a half. The kidneys immediately became red and turgid, as after a simple transplantation; but about half an hour later the state of the circulation became normal, so that no difference could be detected between the transplanted and the normal kidneys. Clear urine flowed abundantly from the transplanted ureters, which were united to the normal ones.

Both normal kidneys were dissected and extirpated. The appearance of the transplanted and normal organs was so similar that in extirpating the latter it was necessary to examine the pedicle in order to be certain of their identity. The operation was completed by suturing the abdominal wall and applying the dressing. Two hours after the operation the animal walked about her cage. In the afternoon she drank and urinated copiously. The following day and subsequently her diet largely consisted of meat. She drank, ate, walked, and, when permitted, mingled with other dogs; but in the latter case she was carefully watched, as she showed a strong disposition to fight. As far as could be detected, her condition was normal. The urine was clear and showed no evidence of containing blood. The total amount appeared to be somewhat increased. On the seventh and eighth days several samples were collected and analyzed, the results of which showed a slight variation in composition, but probably within normal limits. The only abnormal constituent detected was coagulable proteid, the largest amount present in any of the samples being less than 0·25 per cent. A brief result of the analysis is given below:

Urine collected on the eighth day after the operation: Colour, pale yellow; odour, normal; reaction, slightly alkaline; urea, 1·95 per cent.; uric acid, trace; chlorides, sulphates, and earthy and alkaline phosphates, normal; kreatinin, doubtful; indoxyl none; coagulable proteid, less than 0·25 per cent.; sugar and peptone, none (*cf.* p. 242).

It was inconvenient to collect the total urine for twenty-four hours, as it was deemed advisable to allow the animal to move about freely.*

Some of our animals lived for weeks after such operations, but all ultimately died, with well-marked uræmic symptoms. And no

* The above experiment is quoted from a paper by Carrel and the writer in Science, N.S., vol. xxiii., No. 584, p. 394, March 9, 1906.

one, though many experiments have been reported, has yet succeeded in keeping an animal alive for any great length of time which carried the kidney or kidneys of another animal after its own kidneys were removed.

Gross histological examination of kidneys transplanted by the writer showed a congestive, hæmorrhagic, and progressive degenerative process. In the beginning the circulatory change is greatest in the boundary zone, but later the cortex of the kidney presents extensive hæmorrhages and degeneration and disappearance of the renal cells.

There seems to be some variation in the results—*e.g.*, rate and magnitude of the pathological process. But the degenerative pro-

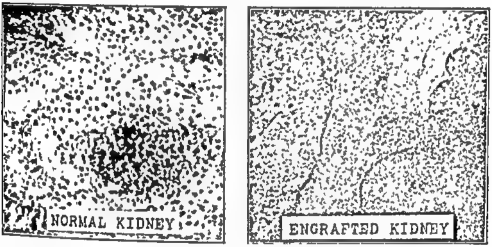


FIG. 104.—COMPARISON OF MICROSCOPICAL APPEARANCE OF THE CORTEX OF THE CAT'S NORMAL KIDNEY, WITH AN ENGRAFTED KIDNEY SEVENTEEN DAYS AFTER THE OPERATION.

cesses are progressive, a seventeen-day specimen showing much more marked degenerative changes than specimens taken after shorter intervals. In all these experiments the kidneys were subjected to complete anæmia and perfusion with saline solution, and these factors have to be taken seriously into account. In a case in which only one kidney was removed from a cat, one kidney from another cat was introduced, and appropriate vascular and ureteral connections made. This animal did well, as shown by a photograph taken about a year later. Her remaining kidney was then removed, and she died in a few days with the usual symptoms of renal insufficiency. Histologically, only traces of normal structure remain, a few glomeruli and tubules having preserved sufficient of their structure for identification. This, so far

as I am aware, is the longest observation which has been recorded on an iso-engrafted kidney, and therefore the longest instance of survival of such engrafted renal tissue.

In addition to the period of complete anæmia with perfusion to which the kidney was subjected at the time of operation, other factors probably contributed to the disappearance of renal tissue. There was more or less ureteral stenosis, but whether this was due to a lack of activity on the part of the kidney or to operative fault is, of course, unknown. The same was true of the renal blood-vessels, and, as in the case of the ureter, the primary factor in producing the condition is unknown. That the kidney still received

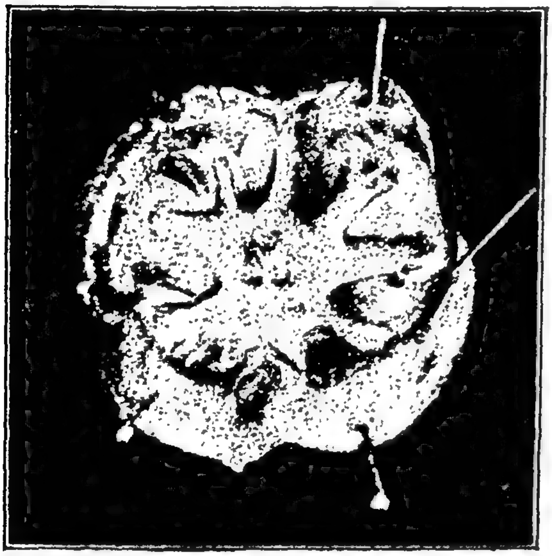


Fig. 105.—Engrafted Kidney at Post-Mortem Examination of Cat.
(*Journal of the American Medical Association*, 1908, li. 1658.)

Fig. 106.—Microscopic Appearance of Kidney shown in opposite Figure.

blood is evidenced, not only by the examination at the time of the last operation, but by the presence of a relatively large mass of tissue; for when the circulation to a kidney is completely shut off, absorption soon occurs.*

Villard and Tavernier have recently reported results of transplanting kidneys without perfusion of their blood-vessels. A kidney was removed from a dog, and the end of the renal artery connected with the carotid artery and the renal vein with the external jugular vein, and the ureter was made to open upon the

* The above experiment is quoted from a paper by the writer in the *Journal of the American Medical Association*, March 12, 1910, liv. 831-831.

surface of the skin. The circulation was interrupted for one and a half hours. The urine secreted by this kidney for a time contained albumin. At the end of fifty-six days there was an abundance of albumin-free urine, and it contained 2·8 per cent. urea.

FIG. 107.—KIDNEYS AND AORTA OF CAT 22, OPERATED ON MAY 23; PHOTOGRAPHED MAY 22, ONE YEAR LATER.

A, Right kidney, rendered anæmic and perfused; B, left kidney, anæmic only; E and D, temporary clamps on aorta; C, showing method of clamping ureteral vessels; F, perfusion needle, thrust into aorta and connected by tube with reservoir holding solution (see pp. 240 and 242).

(*Archives of Internal Medicine*, 1910, v. 232.)

Another operation was performed, and the animal died sixty-eight days after the kidney was first transplanted. At the autopsy the kidney macroscopically was normal, save for a slight nephrosis and thickening of the capsule.

These investigators question the use of salt solution for perfusing kidneys for transplantation—indeed, they systematically abstain in all cases from perfusing. In substantiation of this position, which had previously been pointed out and the reasons in its support advanced by the writer, they cite the paper,* which I am permitted to quote through the kindness of the Editor.

Investigations in this direction were suggested by the character of the results following transplantation of kidneys.

The method consisted in temporarily shutting off the circulation in a segment of the aorta, including the origin of the renal arteries, and then perfusing the kidneys by injecting the solution to be tested into this segment by means of a small trocar (or needle) thrust through the wall of the aorta, the instrument being connected by means of a rubber tube with a reservoir containing the solution (see p. 23).

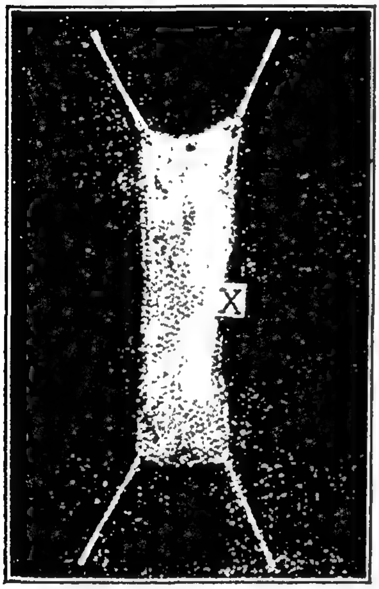


FIG. 108.—SEGMENT OF THE AORTA OF A CAT WHOSE KIDNEYS HAD BEEN PERFUSED BY THRUSTING A TROCAR INTO THE AORTA.

The puncture, which was made near X, is well healed.

On withdrawing the needle the puncture in the wall of the aorta was closed by several simple stitches which penetrated the coats of the vessel. The clamps (serrefines) were then removed from the aorta, and the abdominal wound closed. The animal was then bandaged and placed in the hospital.

It should be remarked that, in addition to the aorta, all arteries other than the renal arising from the segment were clamped, as well as all other vessels that might give a collateral circulation—*e.g.*, the ureters, with their surrounding tissues were compressed in mass by means of encircling coarse ligatures. (Narrow strips of cloth, temporarily fastened by means of ordinary hæmostatic forceps or serrefines, are very good for this purpose.) Even with such precautions, more or less patent connections were maintained, as shown by the fact that on withdrawing the perfusion needle, as a rule, arterial-hued blood soon began to escape from the opening.

In some of the experiments the adrenals were shut off by the anterior serrefines, and sometimes they were not, so that data

* *Archives of Internal Medicine*, 1910, v, 232.

on the results of perfusing them was also obtained. In some cases the renal artery (or arteries) to one kidney was clamped during the perfusion, so that it was possible to compare on one animal the result of anæmia alone with anæmia accompanied by perfusion. The temperature of the perfusion liquid varied in different cases, as noted in the table (p. 244). The pressure employed was, for the

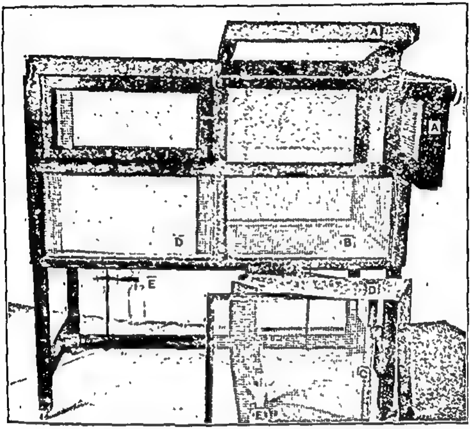


FIG. 109.—PRACTICAL FORM OF METABOLISM CAGE, CONTAINING TWO COMPARTMENTS; ONE COMPARTMENT IS ASSEMBLED; THE OTHER IS OPEN AND DISMOUNTED, TO SHOW INSIDE FEATURES.

A, Hinged door; B, funnel-shaped metal bottom; C, removable metal screen bottom, on which the animal rests; D, metal guard, which fits inside upturned flange on B; E, funnel and bottle for receiving urine. Frame finished with waterproof paint. All metal parts galvanized or tinned.

(*Cf. Archives of Internal Medicine*, 1910, v. 234.)

most part, practically constant for the non-colloidal solutions (plain sodium chloride, Ringer's and Locke's solutions); but with colloidal solutions—*e.g.*, starch—more pressure was required to force the liquid into the capillaries. In those cases in which the urine was collected the animals were kept in metabolism cages along with control cats. The diet, etc., was the same in all cases.

On beginning the perfusion, the kidneys could be observed through their capsules to become paler, the degree of paleness being taken as an index of the degree of perfusion. In addition, puncture of the kidneys was made (also through the capsules) with a very fine needle (No. 14 cambric, the size usually employed for closing the puncture in the aorta), which permitted a minute quantity of liquid from the blood-vessels to escape. By closely observing this liquid as it spread out on the capsule, the presence of red blood-corpuscles could be observed. It is doubtful whether in any instance such liquid was altogether free of such corpuscles. The perfusions, therefore, were relatively, and not absolutely, complete. The same was in general true for the anæmias, though the amount of arterial blood reaching the kidneys was small.

On releasing the temporarily occluded arteries, the kidneys rapidly assumed an appearance indicative of a very active circulation.

In the case of anæmia alone of the kidneys, or of the kidneys and suprarenals together, no abnormal symptoms were observed in the behaviour of the animal, and recovery was uneventful. When one kidney was subjected to anæmia alone, and the other to anæmia with perfusion the result was the same. Anatomically, the changes thus far observed have been less marked when perfusion was not practised.

In the case of Cat 22, in which one kidney was rendered anæmic, while the other was in addition perfused with Locke's solution, a marked increase in size of the former (compensatory hypertrophy ?) with practically complete disappearance of the latter (perfused) kidney was observed 155 days after the operation. Twelve months later the animal was photographed and then killed with chloroform, and the kidneys photographed (see p. 237).

No marked histological alterations have been observed. Eisendrath and Strauss, using rabbits, have confirmed the results as to absence of marked structural alterations in kidneys after short periods of anæmia; but they obtained no results as to the effect of such procedure upon the renal function, as they operated upon but one kidney. And as Wells pointed out in discussing their results, "cells may show extensive histological changes and be functionally competent; and may also show no histological changes, and be totally incompetent." Of great interest in this connection, is Wells's observation that fattily degenerated liver cells showed as great power to destroy uric acid, which is difficult to oxidize, as normal liver cells.

No chemical studies have been made when anæmia alone has been practised. The metabolism of such animals has suffered no marked alteration, as judged by the condition, behaviour, etc.

After anæmia with perfusion of the kidneys, cats as a rule show no unusual symptoms for twenty-four hours or more. During this time they appear the same as any cat on which a major surgical operation has been performed. In the more acute types of cases the usual symptoms of renal insufficiency rapidly develop, terminating in the death of the animal within a week or ten days, while in the slower types such pronounced symptoms do not appear for weeks or months. In all cases where such symptoms have been pronounced, death has invariably occurred within a few days. As a rule death follows the appearance of such symptoms more quickly in the acute than in the slower types of cases. In the latter especially, the animals usually showed great emaciation before death, or even before the onset of convulsive symptoms. With the onset of convulsions, in all cases death occurred within a few days. In the more acute cases the character and train of symptoms were practically indistinguishable from the symptoms following simple ligation of the renal blood-vessels or double nephrectomy. For a day or two preceding death there appeared to be a more or less complete suppression of urine. The pupils usually showed marked constriction during the period of slighter convulsions and during the onset of the stronger ones, but during the height of the stronger convulsions they became dilated. It may be remarked that such changes in the pupils are probably due to deficient respiration, it being known that partial asphyxiation produces a constriction, followed by a dilation, if the asphyxia be sufficiently complete.

As a rule, when examined up to a few weeks after the operation, the grosser anatomical changes consisted in what may be termed a "subnormal resiliency"—*i.e.*, the kidneys feel more or less flabby; in appearance they are pale; on section the cortex is pale, the medulla congested, and in the boundary zone a marked stripe of congestion is seen. The tissue has more or less of the "cooked" appearance that pathologists have associated with parenchymatous degeneration. Ultimately the kidney becomes harder, and on section less medullary congestion is seen. The cortex is paler than normal.

The most prominent histological feature in early examinations is the congestion. This is greatest in the boundary zone and medulla. Later, interstitial hæmorrhages occur throughout the entire organ.

At this stage cloudy swelling, of the tubular cells especially, observed. This, and the succeeding degeneration, is also ve marked in the cortex. Cellular infiltration also occurs, particula in the boundary region. The degenerative process may proceed ur cell structure is lost. As a rule such processes are more mark in certain areas than in others, so that such areas are surrounded tissue showing more nearly normal structure. Such degenerati may result in the disappearance of Malpighian corpuscles as well tubules proper.

Observation on chemical changes were confined to the uri

FIG. 110.—KIDNEYS OF CAT 32, WHICH WERE PERFUSED SALT SOLUTION JANUARY 26.
The animal died February 15, twenty days after po
(*Archives of Internal Medicine*, 1910, v. 2,

At first there seemed to be a de amount urine showed a high specific g h perce solids—*e.g.*, urea and chlorid protr amount and composition mi normal prior to death another chan t the s and content of normal solid the n interesting to note the co al cat daily average for one of r one follows: Amount, 91·4 c.c 1·050

abundant; urea, 17·5 per cent. by the hypobromite method. This figure for urea is unquestionably too high. For some reason the hypobromite method has indicated far too much urea in all cats' urines to which it has been applied.] Neither albumin or sugar have been observed, at least in sufficient quantities. Since the interpretation of such results is a matter requiring care, owing to the great complexity of factors—*e.g.*, amount and composition of the food eaten, liquids drunk, body weight, physiological state, etc.—a more complete discussion is not possible with present data. The metabolism appears to suffer great alterations, as judged not only by changes in the urine, but by loss of appetite and weight and change in general behaviour.

The results show conclusively that renal and adrenal anæmia, coupled with perfusion with all the solutions tried, is much more harmful than anæmia alone. Anæmia alone is certainly not to be looked on as being without effect, but it seems that for cats, under the conditions of these experiments, short periods of occlusion are not incompatible with permanent recovery of the animal. The observations have not been carried sufficiently far to enable us to conclude that the life of the animal is not shortened by the anæmia. Neither may we conclude that anæmia with perfusion as performed, invariably shortens the period of life remaining to the animal; for in few cases, when death did not occur for some months, we cannot be absolutely certain—though the evidence on the whole is strongly in this direction—that death was due to the operation. Carrel, in repeating Chirie and Mayer's work on the effect of temporary occlusion of the renal veins on dogs, observed death in one case in a few months after the operation, the period of occlusion being twelve minutes. He attributed death to *ostéo-périostite* of the atlas.* But it seems simpler to assume that the operation had a share in causing death, since Chirie and Mayer observed epileptiform manifestations and rapid death o dogs in which the renal veins had been occluded for ten minutes. As before indicated, the completeness of the anæmia during the period of occlusion is no doubt an important factor, and better control of this may tend to render the results of different investigators more uniform. In addition to this, however, differences in resistance to anæmia, as well as to anæmia with perfusion, will probably be demonstrated not only in animals of different species, but in individuals of the same species.

For the present, therefore, since all solutions seem to have a toxic

* Carre. *Comp. Rend. de la Soc. de Biol.*, 1909, lxvi. 527.

ABLE OF EXPERIMENTS ON ANÆMIA AND PERFUSION OF KIDNEYS.*

No.	Date operated.	Aorta occluded.		Period perfused.		Solution perfused with—	Death after (Days).	Remarks.
		Min.	Sec.	Min.	Sec.			
16	24/4/08	13	0	11	0	Ringer's	3	Both kidneys perfused.
17	25/4/08	13	0	11	0	Ringer's	9	Both kidneys perfused, nerves cut.
18	29/4/08	11	0	9	0	Ringer's	1	Both kidneys perfused, clot in aorta.
19	7/5/08	13	0	10	0	Ringer's	3	Right kidney *only* perfused.
20	7/5/08	14	0	8	30	Ringer's	2	Both kidneys perfused.
21	23/5/08	15	0	12	0	Locke's	3	Both kidneys perfused.
22	23/5/08	9	45	8	20	Locke's	364	Anæmia of both kidneys, right only perfused. Chloroformed.
23	23/5/08	12	30	0	0	0	40†	Anæmia only of kidneys. Escaped in July in good condition. Showed no symptoms of renal insufficiency.
24	3/11/08	22	0	0	0	0	8†	Anæmia only of kidneys. Cat in splendid condition until eighth day, when abdominal wound opened owing to absorption of gut suture material, allowing the intestines to escape.
25	3/11/08	0	0	0	0	0	2·5	Ligated renal vessels permanently.
26	3/11/08	0	0	0	0	0	6	Excised kidneys.
29	16/12/08	20	35	7	0	0·9 NaCl	84	Partial perfusion only of both kidneys.
30	16/12/08	28	0	16	30	Starch	1·5	Both kidneys perfused.
31	22/12/08	16	0	8	0	0·9 NaCl	131	Left kidney excised.
32	26/1/09	25	0	15	30	0·9 NaCl	20†	Clot in aorta. Some temporary paralysis. Chloroformed after recovery.
33	26/1/09	9	0	4	15	0·9 NaCl	123†	Partial perfusion both kidneys.
34	26/1/09	16	30	12	30	0·9 NaCl	105†	Both kidneys and adrenals.
35	26/1/09	14	10	10	0	Locke's	7	Both kidneys and one adrenal perfused.
36	27/1/09	10	0	2	15	0·9 NaCl	474	Partial perfusion both kidneys.
37	27/1/09	12	30	5	0	0·9 NaCl	101	Partial perfusion both kidneys and suprarenals.
38	27/1/09	10	30	7	0	Locke's	683 (about)	Right kidney removed. Had several litters of kittens. Always very thin, finally became very sick and disappeared.
39	27/1/09	9	0	5	30	Ringer's	36	Both kidneys perfused.
40	27/1/09	11	30	5	30	Ringer's	33	Both kidneys perfused.
41	27/1/09	14	15	9	30	Locke's	32	Both kidneys and adrenals perfused.
42	4/2/09	18	0	12	0	0·9 NaCl	7	Both kidneys and right adrenal perfused.
44	4/2/09	19	30	12	0	0·9 NaCl	14	Both kidneys perfused. Young cat.

* *Journal of the American Medical Association*, 1908, li. 1658, and *Archives of Internal Medicine*, 1910, v. 232.

† Indicates that the animal escaped or was killed. This is usually indicated under "Remarks." Nos. 33 and 34 are exceptions. They were chloroformed after they became too weak to stand. The amount of liquid perfused varied from about 10 to 30 c.c., in general the amount varying with the period of perfusion. In no case, with the possible exception of Cat 30, was the perfusion made with the pressure exceeding an average blood-pressure in cats. The solutions were brought to body temperature before beginning the perfusions in most cases, but when the room was very cold the temperature of the solution was considerably lowered before it entered the blood-vessels. The following temperatures were recorded: For No. 30, 15°; No. 31, 37°; No. 36, 20°; No. 38, 15°; No. 39, 20°; and No. 41, 12° C. These temperatures were taken by allowing the liquid to spurt through the needle on to the bulb of a thermometer.

action, it would be unprofitable to discuss the apparent small differences in the toxicity of the solutions used on the cats (see p. 120).

Borst and Enderlen claim to have observed a dog to live one hundred days or more after one of its own kidneys had been removed and replaced in the abdominal cavity with vascular and ureteral anastomosis, with removal of its other kidney.

No one has as yet reported successful results in transplanting kidneys from one individual to another, even when very closely related individuals have been used, for more than a few weeks; and no one has succeeded in keeping an animal alive with the kidney or kidneys from an animal of a different species for more than a few days. When it is remembered that an animal may survive for a period of ten days or more after removal of its kidneys, the fact that an animal may survive a few days when its own kidneys have been removed and replaced with kidneys from another animal does not indicate that such engrafted kidneys are performing an adequate renal function. Of course, when an animal is permitted to retain one of its own kidneys after such an operation, the fact that it may survive for weeks indicates nothing as regards the functional state of the foreign kidney; for an animal may get along very well indeed with but one of its own kidneys.

Therefore, the only results that speak for a degree of functional activity of engrafted tissues are those observed in animals surviving for weeks after all of their normal renal tissue was removed. From this standpoint it may be concluded from results hitherto reported that a re-engrafted kidney or kidneys may adequately functionate to preserve the life of the animal at least for months. Also it may be concluded that a foreign kidney, even though it be from a very closely related animal of the same species, can only functionate adequately to preserve the life of the animal for at the most a few weeks.

Most investigators agree that an engrafted foreign kidney or kidneys from a different species has not shown evidence of prolonging the life of the host; but since it is now known that the perfusion that has been practised in transplantations is of itself harmful, and since it is known that it is possible to perform the operation so quickly as to render such perfusion for the purpose of preventing intravascular coagulation unnecessary, we may confidently hope for more uniform and permanent results in cases of auto-engrafted kidneys. But from such results only experi-

mental and therefore only indirectly practical benefits may be derived, for auto-renal grafts will, for obvious reasons, never be of direct practical importance; for if the operation is ever applied therapeutically, it will be for the reason that the animal's own renal tissue is deficient or abnormal, and for that reason the operation will be performed with the view of engrafting renal tissue from another animal. Here, again, the obstacle of inadequate survival or adaptation of such engrafted renal tissue is encountered. The outlook is by no means hopeless, but it would not be practicable to enter into a discussion of the probable reasons, or the methods that might be tried experimentally with the view of overcoming the difficulty other than to say that the principles of immunity, which yield such brilliant results in many other fields, would seem to be worthy of being tested in this case.

Results of Transplantation of Thyroid.

For a long time it has been known that thyroid tissues may be successfully engrafted. Schiff and Kocher, in the early eighties, the former using dogs and the latter operating on man, obtained temporary benefit by engrafting after removal of the thyroids. In 1892 Eiselberg reported anatomically and physiologically successful results on cats. A little later Cristiani reported successful results on numerous species of animals. All such transplantations have been performed without anastomosis of the blood-vessels, so that the results have been best when thin masses of tissues have been employed.

With Carrel, in 1905, one thyroid lobe of a dog was removed, and after washing out its vessels with salt solution it was replaced in the situation from which it was taken, and the circulation through it restored by anastomosing the peripheral end of the superior thyroid vein to the central end of the corresponding artery, and the peripheral end of the artery to the central end of the vein, thus establishing a reversed circulation through these vessels. Great swelling of the gland occurred, and some infection ensued, but the swelling soon disappeared and the wound healed. The dog never showed any general symptoms indicative of deranged thyroid metabolism. Two years and nine months lat[illegible] animal, which [illegible]ed by the writer, was killed [illegible] form and t[illegible]en examined.

Anatomically, the left thy[illegible] oderately presented the appearance of [illegible]. The r[illegible]

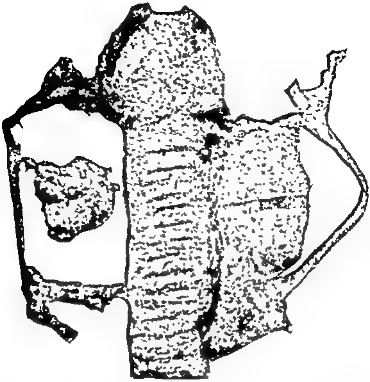
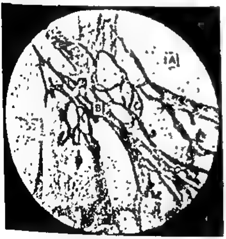


FIG. 111.—RIGHT THYROID LOBE OF DOG, THIRTY-THREE MONTHS AFTER REMOVAL AND REPLACEMENT, WITH REVERSAL OF CIRCULATION IN SUPERIOR THYROID ARTERY AND VEIN.

(Journal of the American Medical Association, 1910, liv. 831.)

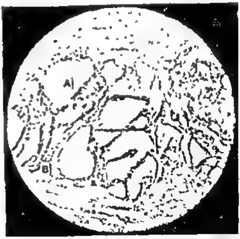


UNOPERATED.

FIG. 112.—MICROPHOTOGRAPH THYROID LOBE (DOG 00), NOT OPERATED ON.

Note large amount of granular colloid (A) and small amount of clear colloid (B), and fibrous relations.

(Journal of the American Medical Association, 1910, liv. 831.)



REPLANTED

FIG. 113.—MICROPHOTOGRAPH THYROID LOBE (DOG 00), OPERATED ON.

Note clear colloid (A) and enormous amount of fibrous tissue (B). No granular colloid.

(Journal of the American Medical Association, 1910, liv. 831.)

quite fibrous and dense to the touch and adherent to surrounding structures. On dissection, the superior thyroid vessels were found intact. Owing to the fibrous adhesions it was difficult to make a satisfactory dissection of the vein. The artery and the point of union of artery to vein is shown in the illustration.

Microscopically, the lobe which had not been operated on presented the appearance of colloidal goitre. The lobe which had been operated on showed an enormously thickened connective tissue capsule. The substance of the gland showed an abundance

Fig. 114.—Autograft from Dog, excised at the Operation of Functional Test, Four Months after its Transplantation. Enlarged $\frac{22}{1}$ (Halsted.)

Death from tetania parathyropriva promptly followed its excision.

(*Journal of Experimental Medicine*, 1909, xi. 175.)

of normal staining colloid. The walls of the acini were considerably thicker than normal, due in part to strands of connective tissue. Otherwise the histologic elements themselves appeared normal, the arrangement only being abnormal. Capelle (p. 16) reports a result indicating functional as well as anatomical survival of a thyroid re-engrafted into a dog's neck. Two hundred and forty-five days after the operation the gland was removed and the dog died in typical post-thyroidectomy tetany.

Results of Transplantation of Parathyroids.

The results of parathyroid transplantations by vascular anastomoses have not been sufficiently studied to consider at this time. Recently, however, Halsted has reported completely successful parathyroid grafting by the simple method.

His results indicate that the survival of an exceedingly small fragment of such tissue seems adequate to prevent the appearance of the symptoms of thyro-parathyroidectomy (tetany, etc.). For example, after transplanting two parathyroid bodies and removing the remainder of the thyroid tissues, the dog remained in good health. Some months later but one of the engrafted parathyroid bodies could be found. This was removed and preserved. "The dog died of tetania parathyropriva on the second (or third ?) day after the operation," thus proving the functional state of the removed autograft. The tissue was microscopically examined, and the results are shown in Fig. 114.

Results of Transplantation of the Heart.

The heart of a small dog was extirpated and transplanted into the neck of a larger one by anastomosing the cut ends of the jugular vein and the carotid artery to the aorta, the pulmonary artery, one of the vena cava, and a pulmonary vein. The circulation was re-established through the heart, about an hour and fifteen minutes after the cessation of the beat; twenty minutes after the re-establishment of the circulation the blood was actively circulating through the coronary system. A small opening being made through the wall of a small branch of the coronary vein, an abundant dark hæmorrhage was produced. Then strong fibrillar contractions were seen. Afterward contractions of the auricles appeared, and about an hour after the operation effective contractions of the ventricles began. The transplanted heart beat at the rate of 88 per minute, while the rate of the normal heart was 130 per minute. A little later tracings were taken. Coagulation occurred in the cavities of the heart after about two hours, and the experiment was interrupted.*

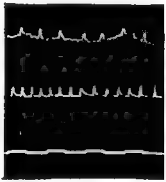


FIG. 115.—RECORD OF CONTRACTIONS OF ENGRAFTED HEART (UPPER TRACING) AND OF ANIMAL'S OWN HEART (MIDDLE TRACING).

The lower tracing shows time.

* This experiment is quoted from a paper by Carrel and the writer in *American Medicine*, December 30, 1905, vol. x., No. 27, pp. 1101-1102.

Transplantation of the Lungs and Heart.

"We attempted also the transplantation of the lungs together with the heart. Both lungs, the aorta, and vena cava of a cat one week old were extirpated and put into the neck of a large adult cat. The aorta was anastomosed to the peripheral end of the carotid, and the vena cava to the peripheral end of the jugular vein. The coronary circulation was immediately re-established and the auricles began to beat. The lungs became red, and the ventricle began to contract strongly; but œdema of the lungs soon appeared and the right heart became distended. Owing to infection the examination was discontinued two days later."*

Results of Transplantation of the Head.

May 21, 1908.—Moderate-sized dogs used.

2.35 p.m.: Etherized.

3.18: Head to be engrafted was amputated.

3.25: Common carotid artery of right side of host was anastomosed to same vessel on left side of engrafted head.

3.36: External jugular vein similarly anastomosed.

3.47: Circulation restored; period of anæmia in engrafted head was twenty-nine minutes.

4.18: Operation completed (muscles, skin, etc., sutured); ether removed. The following observations refer to the engrafted head:

4.30: First movement of nostrils noticed, indicating respiratory discharge; tongue twitching; colour of tongue is pink.

4.31: Respiratory movements about 2 per minute.

4.32: Pupils contracting.

4.37: Respiratory movements continue at intervals of about eleven seconds.

4.39: Muscles of the throat contract with respiratory effort.

4.46: Lids closed; pupils contracted; respiratory movements continue; tip of nose moist; tongue and mucous membrane red.

4.50: Gasping movements.

4.57: Muco-sanguineous fluid is discharged from nostrils; pupils very small.

5.12: Respiratory movements 10 per minute; respiratory rate of host 60 per minute.

5.17: Copious flow of saliva; none in host.

* *Johns Hopkins Hospital Bulletin*, 1907, xviii. 25.

5.27: Pupils contracted; fibrillary twitching of tongue, which is retracted completely; jaws close when not restrained; respiratory movements stronger, and rate 14 per minute.

5.31: Secretion of tears and copious salivation.

5.45: Temperature of both heads is 38° C.

6.00: Pupils less contracted.

6.03: Slight secretion of saliva from host.

6.37: Respiratory rate of host 30 per minute; respiratory rate of engrafted head 24 per minute; respiratory movements are more gentle in character; right pupil has been dilated a short time, while left pupil has remained well contracted. Saliva still flowing; tongue not so greatly retracted, and fibrillary contractions less active than before.

6.55: Pupils as before; respiratory movements of nostrils have disappeared; "boiling movement" of tongue.

7.00: Respiratory rate of host 27 per minute, and deep.

7.05: Circulation in engrafted head very active; no movements observed, but saliva is still flowing.

8.35: Temperature of both heads is 36° C.; both pupils now dilated; circulation remains good.

8.50: Respiration in host 16 per minute; physical conditions good.

9.40: Respiration in host 14 per minute; pulse 178.

9.50: Drank water.

3.07 a.m.: Drank water; respiration 18½ per minute; pulse 147; animal seems more animated.

6.28: Circulation good in engrafted head; respiration in host 21 per minute; pulse 132.

8.23: Vomited some pale greenish fluid.

9.40: Respiration becoming laboured.

10.02: Respiration more laboured; etherized animal.

10.08: Opened neck; soft clot was found in the vein, which disappeared on slight manipulation; arterial pulse good; wound good; only small amount of serous fluid escaped.

10.26: Muscles of engrafted tongue and neck contracted when stimulated directly with induced current; tongue shows "boiling movement."

Etherized animal.

May 27, 1908.—Two animals of same size were taken; weight of host was 14 pounds.

Central ends of the carotid arteries and the central ends of the

internal jugular veins were anastomosed to the peripheral ends of corresponding vessels of the head to be engrafted. This was done before removing head.

3.21 p.m. : Neck and spinal cord severed. Began sewing muscles and skin of transplanted head to skin and muscles of host.

The following observations refer to the transplanted head:

3.22 : Gasping movements, with twitching about mouth.

3.27 : Gasping movements, with strong retraction of tongue. Respiratory efforts ; eye reflex absent.

3.32 : Operation completed ; engrafted head quiet ; anæsthetic discontinued.

3.49 : Respiratory efforts again begin in head ; pupils diminishing in size.

4-5 : Animal demonstrated at a meeting of physicians and surgeons.

During this period the engrafted head gave evidence of aural, visual, and cutaneous reflex movements.

5.42 : Pupils small ; lid reflex good ; makes respiratory efforts and gasps ; no salivation.

6.13 : Lid reflex good ; pupils dilated ; mouth dry.

6.27 : Lid reflex absent ; respiratory movements absent ; circulation excellent.

6.40 : Animal etherized ; clamped arteries to engrafted head. This was followed by fibrillary twitching of the tongue and contraction of the muscles of the neck ; also gasping movements. Animal killed, as the operation was not performed aseptically.

Results of transplantation of the head have been discussed in a preceding chapter (p. 116).

REFERENCES.

ABBE: N. Y. Med. Journ., 1894, lix. 51.
BLUNDELL: Physiol. and Path. Researches, London, 1825.
BORN: Quoted by Morgan, Regeneration, 1907, 182.
BORST AND ENDERLIN: D. Z. f. Chir., 1900, 54.

BOYCOTT AND DOUGLAS: Jr. of Path. and Bact., 1909, xiii. 256; *ibid.*, 1910, xiv. 294.
BRADFORD: Jr. of Phy., 1889, x. 358; *cf.* Stewart, Manual of Physiol., 1910, 569.
BROOKS: Heart, 1910, ii. 35; Jour. Am. Med. Assn., 1910, lv. 373.
BROWN, O. H.: Science, N.S., 1909, xxix. 824.
BROWN SÉQUARD: Archives Générales, 1858, 107.
CARRELL: J. H. H. Bul., 1907, xviii. 18; C. R. de la S. de B., 1909, lxvi. 527.
CARRELL AND GUTHRIE: Science, N.S., xxii., 1905, 473, 565; 1906, xxiii. 394, 584; C. R. de la S. de B., 1905, lix. 412, 413, 596, 669; 1906, ix. 378, 465, 466, 529; lxi. 276; Am. Jr. of the Med. Sc., 1906; Annals of Surg., 1906, xliii. 203; S. G. and O., 1906, ii. 266; Amer. Med., 1906, x. 1102.
CASTLE: Science, N.S., 1909, xxx. 312.
CHIRIE AND MAYER: C. R. de la S. de B., 1907, lxii. 598.
COOPER: Surgical Papers, 1845, 170.
CRISTIANI: Comptes Rendus Soc. de Biol., 1894, 716; Journ. de Physiol. et Path. Générale, 1901, 204; *ibid.*, 1904, lvi. 194; Jour. de Physiol. et Path. Gén., 1905, vii. 264.
CRILÈ: Jr. of the Am. Med. Assoc., 1906, xlvii.
DARWIN: Variations in Animals and Plants (John Murray), London, 1899.
DENYS: Dictionnaire de Médicin, xxix. 738.
EISELBERG: Wien. Klin. Wochensch., 1892, No. 5, 81.
EISENDRATH AND STRAUSS: Jr. of the Am. Med. Assoc., 1910, lv. 2286.
FLORESCO: Jr. de Physiol. et de Path. Générale, 1905, vii. 47.
FOSTER: Hist. of Physiol.
GALTON: Proc. of the Royal Soc., 1871. Quoted by Romanes.
GARRÈ: Deutschen Medizinischen Wochenschrift, 1909, No 40.
GARTNER: Quoted by Darwin, *loc. cit.*, ii. 434.
GIES: Amer. Jour. of Physiol., 1902, vi. 53.
GUTHRIE, C. C.: Jour. of Exp. Zool., 1908, v. 563. See also Archives Internationales de Physiologie, 1907, v. 108; Proc. of the Soc. for Exp. Biol. and Med., 1910, vii. 43, 44, 151; Science, N.S., 1909, xxx. 724; Am. Jr. of Phys., 1907, xix. 16; J. of Exp. Med., 1910, xii. 269; Heart, 1910, ii. 115; Jr. of the Am. Med. Assoc., 1908, li. 1658; 1910, liv. 831; Wash. Univ. Bul., 1908, vii. 40; Ar. of I. Med., 1910, v. 232; Zeitschrift für Biologische Technik und Methodik, 1911, ii., No. 3; Proceedings of the International Assn. of Instructors and Investigators in Poultry Husbandry, 1911.
GUTHRIE, C. C., AND RYAN, A. H.: Interstate Med. Journ., 1911, xviii. 167.
GUTHRIE, C. C., GUTHRIE, F. V., AND RYAN: Science, N.S., 1910, xxxi. 395.
HALSTED: Jr. of Exp. Med., 1909, xi. 175.
HARPER: Quoted by Patterson.
HARRISON: Jour. of Exp. Zoology, ix. 799.
HEKTOEN AND CARLSON: Journ. of Infectious Diseases, 1910, vii. 319.
HOWE: Med. Sc., 1889, vii. 214.
HUBER: Deutsche Medizinische Wochenschrift, 1910, xxxvi. No. 23.
JOEST: Quoted by Morgan, Regeneration, *loc. cit.*
KELLOG: Science, 1911, xxxiii. 783.
KOCHER: Cor-Bl. f. Schweiz. Aerzte, 1895; quoted by Vincent, *Lancet*, London, Aug. 11 and 18, 1906.
LABVRIES: Cyclopædia of Practice of Medicine, Am. ed., iv. 468.
LAMBERT AND HANES: Jour. of Exp. Med., 1911, xiv. 129.
LEWIS AND LEWIS: Jour. of Johns Hopkins Hospital *Bulletin*, 1911, xxii. 126; Jour. Amer. Med. Assn., 1911, lvi. 1795.

LOEB, J.: Quoted by Morgan, *loc. cit.*, 182, 184.
LOWER: History of Physiology (Foster), University Press, Cambridge, 1901, 181.
LYON: Amer. Jour. of Physiol., 1909, xxv. 199.
MAGNUS: Norsk Magazin for Lægevidenskaben, 1907, No. 9.
MORGAN: Regeneration, 1907, 173; Experimental Zoology, 1907, 178-181; *ibid.*, 1907, 285.
MORPURGO: Ar. di Fisiologia, 1908, vi. 27.
NEWPORT: Quoted by Darwin, *loc. cit.*, ii. 356.
PATTERSON: Science, N.S., 1909, xxix. 825.
POLICARD: Jr. de Physiol. et de Path. Générale, 1908, x. 240.
QUATREFAGES: Quoted by Darwin, *loc. cit.*, ii. 356.
ROMANES: Darwin and After Darwin, 1906, ii. 145, 148.
SAUERBUCH AND HEYDE: Zeitschrift für Experimentelle Pathologie und Therapie, 1909, vi. 33.
SCHIFF: Rev. Méd. de la Suisse Rom., 1884, 438; quoted by Vincent, Lancet, London, Aug. 11 and 18, 1906.
STEINACH: Quoted Jahr. Physiologie, 1895, iii. 79, 85.
ULLMANN: Wiener Klinische Wochenschrift, 1902, xv. 281.
VILLARD AND TAVERNIER: Presse Médicale, 1910, xviii., No. 52.
VINCENT: Lancet, London, Aug. 11 and 18, 1906.
WALKER: Quoted by Tigerstedt (Murlin), 1906, 693.
WATTS: J. H. H. Bul., 1907, xviii. 153.
WELLS: Jr. of the Am. Med. Assoc., 1910, lv. 2290.

Summary of Literature on Ovarian and Testicular Transplantation.

1890. Heape: Transferred segmenting ova from fertilized rabbits to the Fallopian tubes of other rabbits, and obtained offspring. Proceedings of the Royal Society, 1890, xlviii. 457; 1897, lxii. 178. Quoted by Vernon.

1894. Romanes: During the twenty years preceding 1894, he transplanted ovaries of newly-born individuals belonging to different well-marked breeds in rabbits and bitches. He was never able to get the foreign ovary or any portion of it to survive. Romanes, "Darwin and After Darwin," 1906, ii. 143-144.

1895. Lode: Observed preservation of structure and numerous spermatozoa in intraperitoneal and subcutaneous fowl testicular autografts. *Wiener Klin. Wochenschr.*, 1895, 345.

1896. Knauer: Results indicated that rabbit testicular autograft in neighbourhood of normal location retains functions. *Centralbl. f. Gynaek.*, 1896, No. 20, 270.

1896. Knauer: Good preservation of histological structure in rabbit ovarian autograft. *Centralbl. f. Gynaek.*, 1896, 270; *Arch. f. Gynaek.*, lx. Isografts unsuccessful.

1897. Dudley: Successful human ovarian isograft. Quoted by Marshall and Jolly. Transactions of the Royal Society of Edinburgh, xlv. 3, 595.

1897. Gregorieff: Successful rabbit ovarian autografts and isografts. Pregnancy resulted in four of the former cases. *Centralbl. f. Gynaek.*, xxi., quoted by Marshall and Jolly, *loc. cit.*

1898. Ribbert: Preservation of structure in guinea-pig ovarian autografts. Temporary transformation of central part of graft into connective tissue during first month, with subsequent return of follicles in core. *Arch. f. Entwick. Mechanic.*, 1898, vii. 668.

1898. Ribbert: Observed rapid degeneration of engrafted testicle. Quoted by Marshall and Jolly, *loc. cit.*

1899. Glass: Successful human ovarian isograft. *Medical News*, 1899; quoted by Marshall and Jolly, *loc. cit.*; Magnus, *Norsk Magazin for Laegevidenskaben*, No. 9, 1907.

1899. Herlitzka: Engrafted triton testicular tissue into peritoneal cavity. *Arch. f. Entwickelungsmech.*, 1899, ix. 1, 140.

1899. McCone: Parturition after rabbit ovarian isograft, with removal of the host's ovaries. Also successful (?) ovarian heterograft (dog on rabbit). *American Journal of Obstetrics*, 1899.

1899. Rubenstein: Evidence of preservation of internal secretory function in rabbit ovarian grafts. *St. Petersburg Med. Wochenschr.*, 1899, 381; quoted by Magnus, *loc. cit.*

1900. Foá: Observed degeneration of engrafted rabbits' testicles *Archives Ital. de Biol.*, 1900, 337.

1900. Foá: Preservation of function and structure in rabbit embryonic ovarian isografts. Such tissue engrafted into a male grows for a time, but between the 90th and 170th day it degenerates. *Arch. Ital. de Biol.*, 1900, 364.

1900. Herlitzka: Good preservation of structure in but one out of forty guinea-pig ovarian isografts. Engrafted ovarian tissue into males. Believes that ovarian autografts will live. *Arch. Ital. de Biol.*, 1900, 89.

1900-1903. Schultz: Successful (?) ovarian heterografting (guinea-pig into mole). *Centralbl. f. allgem. Path. u. Anat.*, 1900, xi.;

1897. Dudley: Successful human ovarian isograft. Quoted by Marshall and Jolly. Transactions of the Royal Society of Edinburgh, xlv. 3, 595.

1897. Gregorieff: Successful rabbit ovarian autografts and isografts. Pregnancy resulted in four of the former cases. *Centralbl. f. Gynaek.*, xxi., quoted by Marshall and Jolly, *loc. cit.*

1898. Ribbert: Preservation of structure in guinea-pig ovarian autografts. Temporary transformation of central part of graft into connective tissue during first month, with subsequent return of follicles in core. *Arch. f. Entwick. Mechanic.*, 1898, vii. 668.

1898. Ribbert: Observed rapid degeneration of engrafted testicle. Quoted by Marshall and Jolly, *loc. cit.*

1899. Glass: Successful human ovarian isograft. *Medical News*, 1899; quoted by Marshall and Jolly, *loc. cit.*; Magnus, *Norsk Magazin for Laegevidenskaben*, No. 9, 1907.

1899. Herlitzka: Engrafted triton testicular tissue into peritoneal cavity. *Arch. f. Entwickelungsmech.*, 1899, ix. 1, 140.

1899. McCone: Parturition after rabbit ovarian isograft, with removal of the host's ovaries. Also successful (?) ovarian heterograft (dog on rabbit). *American Journal of Obstetrics*, 1899.

1899. Rubenstein: Evidence of preservation of internal secretory function in rabbit ovarian grafts. *St. Petersburg Med. Wochenschr.*, 1899, 381; quoted by Magnus, *loc. cit.*

1900. Foá: Observed degeneration of engrafted rabbits' testicles *Archives Ital. de Biol.*, 1900, 337.

1900. Foá: Preservation of function and structure in rabbit embryonic ovarian isografts. Such tissue engrafted into a male grows for a time, but between the 90th and 170th day it degenerates. *Arch. Ital. de Biol.*, 1900, 364.

1900. Herlitzka: Good preservation of structure in but one out of forty guinea-pig ovarian isografts. Engrafted ovarian tissue into males. Believes that ovarian autografts will live. *Arch. Ital. de Biol.*, 1900, 89.

1900-1903. Schultz: Successful (?) ovarian heterografting (guinea-pig into mole). *Centralbl. f. allgem. Path. u. Anat.*, 1900, xi.;

Marshall and Jolly, *loc. cit.* In female porpoises of the same species with engrafted ovaries eggs were laid and corpora lutea formed; in females of different species with engrafted ovaries no changes were observed in the first eight days. In males of same species engrafted ovarian tissue was found to be sound 117 days after the operation. *Monatschr. f. Geburtshilfe*, xvi. 6; *Centralbl. f. Physiologie*, 1903, 174.

1903. Morris: Reported successful rabbit ovarian isografts, function and structure being preserved for some months, but ultimately degeneration occurred. *American Journal of Obstetrics*, 1903.

1904. Limon: Observed follicular degeneration, but preservation and recuperation of vitality by interstitial cells in rabbit ovarian autografts. Quoted by Marshall and Jolly, *loc. cit.*

1904. Shattuck and Seligmann: Preservation of function, including formation of spermatozoa by fowl testicular autograft. Fragments of testicle were accidentally left in the peritoneal cavity in attempts to castrate. Quoted by Marshall and Jolly, *loc. cit.* (This is a common occurrence with unskilled caponizers, and has been known among poultrymen for a long time.—C. C. G.)

1905. Basso: Preservation of histological structure in rabbit and guinea-pig ovarian autografts; degenerative changes in isografts. *Arch. f. Gynaek.*, lxxvii. 51.

1905. Charrin, Moussu, Le Play: Placed testicles in vaginal cavity. Result: atrophy of seminal tubules, etc. *Bulletin Soc. Anat. Paris*, Ann. lxxxi. 394; quoted from *Bibliog. Physiol.*, 1906, ii., iv. 247.

1906. Bond: Modified structure in rabbit ovarian autograft after one month. Quoted by Marshall and Jolly, *loc. cit.*

1906. Cramer: Evidence of preservation of internal secretory function in human ovarian isograft. Return of menstruation and secretion of colostrum by breasts of host. *Sitz. Ber. Natur. Hist. Ver. Preuss. Rheinl. Westphalen*, xxxv., xxxvi., 1906; *Münchener Med. Wochenschr.*, September 25, 1906.

1906. Morris: Reported birth of child in woman from whom ovaries were removed, and into whom an ovary from another woman was engrafted four years previously. *Medical Record*, 1906.

1907. Guthrie: (1) Demonstrated that transplanted ovaries in fowls survive and function; (2) that resulting offspring show evidence of foster-mother influence. Proceedings of the Society, *American Journal of Physiology*, xix., xvi-xvii, July, 1907; *Archives Internationales de Physiologie*, 1907, v. 108; *Journal of Experimental Zoology*, v. 563-576, June, 1908. *Cf. Journal of Experimental Medicine*, 1910, xii. 269. Results of subcutaneously engrafted ovarian and testicular tissue. Proceedings of the Society of Experimental Biology and Medicine, 1909, vii. 43.

1907. Marshall and Jolly: Evidence of preservation of internal secretory function and good preservation of structure in rat ovarian autografts. Also review of literature. Transactions of the Royal Society of Edinburgh, xlv. 3, 589.

1907. Magnus: Good preservation of structure, internal secretory function, and reproductive function in rabbit ovarian isograft. Twenty-five rabbits were operated, and eleven survived. Of this number, but one became pregnant. She was black, and carried ovaries from a white individual, her own ovaries having been removed. Five months after the operation she was bred to a white buck. Of the two resulting offspring, one was white, the other black. Being bred again in the same way, she died shortly before full term. Of the seven young *in utero*, two were solid black and five albinos. Thus, evidence of "soma" or "foster-mother" influence was shown. At post-mortem, the left ovary could not be found. The right ovary appeared almost normal, excepting for rather extensive adhesions. It contained seven corpora lutea in the regressive stage. A review of the literature is given. *Norsk Magazin for Laegevidenskaben*, No. 9, 1907.

1908. Marshall and Jolly: Rat ovarian isografts were also found to be successful. These investigators concluded that—(1) ovarian autografts succeed better in the kidney than in the peritoneal cavity; (2) ovarian isografts succeed less readily than autografts; (3) isografts are more successful between nearly related than between distantly related individuals; (4) it is not necessary to create a deficiency—*i.e.*, remove ovarian tissue—in order to achieve such success. *Quarterly Journal of Experimental Physiology*, 1908, i. 2.

1909. Castle: Obtained young from guinea-pig with engrafted ovaries. *Science*, 1909, xxx. 312-313.

1909. Guthrie: Obtained young from guinea-pig with engrafted ovary. *Science*, 1909, xxx. 724-725.

1909. Guthrie: On graft-hybrids. *Annual Report of the Amer. Breeders Assn.* for 1909, vi. 356, 1911.

1910. Davenport: Inheritance of plumage colour in poultry. Proceedings of the Society for Experimental Biology and Medicine, 1910, vii. 168.

1910. Guthrie: Survival of engrafted ovaries and testicles. *Jour. of Exp. Med.*, 1910, xii. 269.

1910. Sauvé: Ovarian transplantation. *Ann. Gynéc. and Obstétr.*, vii. 155.

1910. Higuchi: Ovarian transplantation. *Arch. Gynakol.*, 91, 214.

1911. Castle and Phillips: On germinal transplantations in vertebrates. Carnegie Institution of Washington, No. 144.

1911. Guthrie: On evidence of soma influence on offspring from engrafted ovarian tissue. *Science*, N.S., xxxiii. 856.

1911. Castle: On "soma influence" on ovarian transplantations. *Science*, N.S., 1911, xxxiv. 113.

1911. Guthrie: Transplantation of germinal elements in poultry. Proceedings International Association of Instructors and Investigators in Poultry Husbandry, 1911.

INDEX

:iginal Index for Dr. Guthrie's book is reprinted exactly as it was, gh certain portions of the text (pages 132-63, 164-92, 193-222, 252- ıd 300-49) to which references are made have been deleted. (See luction by Dr. Samuel P. Harbison, page xii.)

FIFTY YEARS OF VASCULAR SURGERY

BY

BERNARD FISHER, M.D.

COLLECTIVE REVIEW OF VASCULAR SURGERY TO THE PRESENT

I.

THE history of vascular surgery for almost four decades after the original publication of Dr. Guthrie's book is, for the most part, a story of the experience, or rather the lack of success, with this facet of surgery accrued from the battlefields of the world during two Great Wars. Except for a few isolated contributions, the peacetime interval of the twenties and thirties, probably influenced by the failures of World War I, was not a particularly productive or imaginative period in the further development of this type of surgery. The more optimistic of all generations have acknowledged certain scientific, social, and economic advances as valuable by-products of wars. No such dividends seem to have been forthcoming insofar as vascular surgery is concerned.

Of necessity, the treatment for acute arterial injuries in World War I was arterial ligation. Sir George Makins, (305)* who was the chief chronicler of blood vessel surgery performed in the British Army and who reported on over 1,200 cases of vascular injury, stated:

> *I regret not being able to give any information regarding the treatment of gunshot* wounds of the arteries by direct suture. In the cases I myself have seen, the nature of the defect in the arterial wall, the condition of the surrounding tissues, or the fact that the septic condition of the primary tract afforded small hope of performing an aseptic operation, militated against the choice of this method.

Bernheim, (22) who was a devotee of the techniques of direct blood vessel anastomosis in civilian practice, enthusiastically went overseas with his own equipment prepared to carry out vessel suture in battle casualties. Apparently he met with frustration for, in 1920, he recorded his and the experiences of American military surgeons in general by writing:

> Opportunities for carrying out more modern procedures for the repair or reconstruction of damaged vessels were conspicuous by their absence . . . not that the blood vessels were immune from injury or that gaping arteries and veins could not be sutured, but it would have been foolhardy to have tried to suture arteries or veins in the presence of such infections as were the rule in practically all the battle

**Figures in parentheses refer to Bibliography, which follows.*

wounded. Certain isolated successes will be reported without a doubt, but the teachings of Carrel, together with the laboratory experiences of his followers, have so effectually demonstrated the futility of attempted blood vessel suturing in any but a non-infected field that it needed but a glance at the type of wounds to be dealt with to realize from the onset the hopelessness of finer blood vessel surgery. Excision and ligation were the rule and this was rather distressing, particularly when only the side of the vessel had been injured or when the continuity could have been re-established by simple end-to-end suture. It required a high order of self restraint to forego some of these cases.

This was the state of affairs during World War I.

Aside from the large number of amputees resulting from acute arterial ligation, an interesting controversy developed as to whether or not the concomitant vein should be ligated in those circumstances where acute arterial ligation was indicated. This controversy extended unsettled through the post-war period of World War I and beyond the Second World War. As DeBakey and Simeone (108) have commented, it would seem that the amount of space in the literature devoted to thi discussion is out of proportion to the value of the procedure. Befor World War I, surgeons of repute felt that to ligate the vein only worsened the situation. (236) In 1916, a German medical officer, Sehrt, (422) observed that in the lower extremity when the vein was ligated with the artery only 9 per cent of the cases developed gangrene in contrast to 20.4 per cent when the artery alone was tied. The next year, Propping, (387) another German Army surgeon, confirmed these findings. Independently, in his Hunterian Lecture of 1917 and at an Interallied Conference on Military Surgery in Paris on May 17, 1917, Makins, (306, 307) whose prestige and viewpoint were practically unchallenged, felt that to simultaneously ligate the concomitant view had much to offer. It was his opinion that the patent vein permitted too free an exit for the decreased arterial inflow, as well as an undesirable reservoir of stagn tion, and that by ligating the vein, arterial blood that did enter th extremity remained in contact with the tissues for a longer period o time, thus permitting more complete oxygen desaturation. Needless to say, total unanimity of this idea never held sway, but the dissenters, (317, 318, 338, 349, 483) as is usually the case when popular opinion gains momentum and becomes accepted as gospel, were overwhelmed for a time, so that during and following World War I numerous clinical and experimental papers were published substantiating this procedure. (22, 24, 40, 41, 75, 176, 217, 335) Brooks, (39) in reviewing this subject in 1929, concluded that venous ligation had a place only if axillary or popliteal arteries were concerned, but not when the femoral or brachial arteries were involved.

This was the position of concomitant venous ligation with the advent of World War II. *By its termination, however, the procedure* was on less firm footing, for DeBakey and Simeone, (108) in a review of the *results of arterial wounds* in World War II, concluded that ligation of the companion vein furnished no protection against the development of gangrene after acute arterial occlusion. Subsequent experimental work using newer techniques for determination of blood flow failed to confirm some of the earlier results. (88) As recently as 1951, Simeone, Grillo, and Rundle, (439) completely reviewing this subject and feeling that the problem appeared to be far from settled, conducted experiments with cats and concluded that whether the artery is intact or interrupted, or whether the experiment is acute or chronic, ligation of the concomitant vein results in no improvement in muscle function. Further, they felt that conclusions from clinical and experimental evidence favoring ligation of the concomitant vein where a major artery was interrupted were "either unwarranted or subject to different interpretation."

With the onset of the Korean War *the problem of concomitant* venous ligation once more came to the fore, as it did in the previous *World Wars, but in a different fashion.* All observers agreed that where the concomitant vein of an extremity was ligated because of injury to both the artery and vein there was a delay in the return of that extremity to normal after arterial repair. (493) No mention of elective concomitant venous ligation was made in the reports of vascular surgery during this conflict. (235, 493)

There the situation rests—probably forever—for it is now only of historical import. With the resurgence on firm footing of vascular repair by direct suture and the use of vessel grafts to replace defects in continuity, there would seem to be little reason to revive this controversy.

Vascular surgery during World War II has been thoroughly described and evaluated by DeBakey and Simeone. (108) As in World War I, the theoretical value of blood vessel *suture was recognized,* but just as Makins, Bernheim, and others had proclaimed 25 years previously, so did DeBakey and Simeone report:

> . . . it is clear that no procedure other than ligation is applicable to the majority of vascular injuries which come under the military surgeons' observations. It is not a *procedure of choice.* It is a procedure of stern necessity for the basic purpose of controlling hemorrhage because of the location, type, size, and character of most battle injuries of the arteries.

Of 2,471 arterial wounds, suture repair was performed in only 81 cases; of these but three were end-to-end anastomoses.

Although Guthrie and others prior to World War I had suggested the insertion of sutured or non-sutured vein grafts as a method of arterial repair, no information is available concerning their use to bridge gaps in arteries during the World War I period. Such grafts were employed with some success in the treatment of traumatic aneurysms by Goodman (177, 178) of this country and by French (392, 425) and German (222, 468) military surgeons.

In 1942, Blakemore, Lord, and Stefko (32) employed the principle of non-suture anastomosis as developed by Payr, 1900 (387); Höpfner, 1930 (218); and Lexer, 1907 (288). They first lined vitallium tubes with vein grafts and tied the cut ends of the artery over the ends of the cannulae; later they used two short tubes bridged by a vein graft. They were greatly enthusiastic over the possibilities of this technique for restoring blood vessel continuity, particularly in military surgery. DeBakey and Simeone (108) in reporting the use of such techniques during World War II were less than encouraging.

The sporadic use of various prostheses—silver tubes in World War I, (460) or glass (316) and plastic (108) in World War II—failed to leave much of an impression.

That ligation for arterial injuries had still not become outmoded was, as recently as 1952, emphatically dramatized by a report (235) from the Korean War. Until April of that year, ligation of transected vessels was almost as routine as it had been in the prior conflicts, resulting in an amputation rate of 62 per cent. Then, quite suddenly, a new era in traumatic vascular surgery became established. Based upon recent advances in civilian blood vessel surgery, a formal study was initiated by a Surgical Research Team sent to the Korean Theater to attempt to improve upon the situation. The next 75 consecutive arterial injuries in patients unselected except for their ability to withstand surgery were subjected to primary repair, i.e., anastomosis, transverse suture, or vein graft. The amputation rate fell from 62 per cent to 7 per cent—truly a remarkable accomplishment.

II.

It is not implied that blood vessel surgery of that era (1912 to 1950) was concerned only with acute trauma of arteries and ligation management. Indeed, blood vessel suture and anastomosis in this period attracted the attention of many surgeons and frequently took expression in procedures which either have become historically obsolete or have failed to survive under scrutiny. Diversion of arterial blood into venous

pathways of the limb was one of the latter which occupied a prominent place in the literature of the time. In spite of the condemnation of this idea by Guthrie who had extensive experimental experiences, many investigations, both clinical (20, 175, 289, 316, 333) and experimental, (219, 221, 442) were reported until 1916. Although popularity varied, numerous accounts of success with this procedure were published, (20, 23, 123, 175, 289, 332) and sporadically through the years renewed interest was observed. (23, 123, 302, 388) In 1949, however, Leger (278) in France and Jordan (247, 249) in this country renewed real interest in the problem. Szilagyi and his associates (449) extensively reviewed the subject in 1951 and concluded on the basis of experiences with nine patients having occlusive disease of the lower extremities that such a procedure was unjustified and of no value—forty years after Guthrie had already reached this conclusion.

It is of interest that more recently arterialization of the venous system of such organs as the heart, (12, 14, 321) liver, (152, 153) and brain (13, 327) have attracted experimental and clinical attention. To date, there is little or no evidence to suggest that these procedures will ever have a significant place in our therapeutic armamentarium.

The contributions of Rudolph Matas (312) during this period are not to be overlooked. Although progress has relegated the procedure of endo-aneurysmorraphy as described by him to almost complete obsolescence, his rebellion against the classical Hunterian operation of ligating the main artery outside aneurysms of the extremities by replacing the ligature with the suture was a step forward. His application of this principle to the treatment of arteriovenous aneurysm, i.e., the intrasaccular suture of the communicating orifice by the intravenous route (313) (a method which, incidentally, was first described by Bickhan (25) in 1904), came at a time when the "ultra radical" French School of Surgeons, headed by Delbet, (314) was utilizing quadruple ligation to manage them. Interest in this vascular problem continued through the twenties, just as Bernheim (22) had predicted during World War I, when he said:

> . . . most of it [blood vessel surgery] will be done in the years to come when aneurysms of various sorts will begin to crop up, the aftermath of vessels wounded in France in youth, but able to hold their own and carry on until age and perhaps hard work caused trouble in the weak spot.

It was during this period that Emil Holman (213-216) and others (44, 391) contributed much of what we know today about the pathologic and physiologic alterations produced by arteriovenous aneurysm.

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Aneurysm of the aorta defied the needle and thread. Matas (315) did not discard the ligature for the suture in its treatment. He is credited with the first successful ligation of the abdominal aorta for an aneurysm in 1923. Delorme, (111) in 1921, advocated "stripping the nervous network over the aneurysm for the relief of pain," and in that same year Tuffier (462) not only recommended sympathectomy, but also wrapping of the aneurysm with fascia lata. He commented: "Progress in this line is slow, as clinicians do not trust these patients to the surgeons."

Indeed, it was slow, for thirty years passed before DuBost, Allary, and Oeconomos (130, 131) in 1951 first resected an abdominal aneurysm and inserted a homograft. During the interval, insertion of wire into the aneurysmal sac, as first described by Moore (339) in 1864, and the passing of an electric current through the wire to better effect thermal coagulation, as described by Corradi (74) in 1879, were popular. (27, 29, 113, 199, 292) Likewise, wrapping with cellophane containing dicetylphosphate (113, 384) and the use of other materials (19, 113, 181, 301) to produce progressive fibrosis by tissue irritation had their advocates.

In this period several new areas which were destined to importance in the growth of blood vessel surgery had their inception. Notably, these were angiography and the use of anticoagulants.

Opacification of parts of the cardiovascular system began in 1923 when Sicard and Forestier (438) injected iodized poppy seed oil (lipiodol) into peripheral veins of humans. In June, 1924, Brooks (38) of St. Louis injected sodium iodide directly into a patient's femoral artery and produced an opacification—the first successful arteriogram. Three years later, Moniz, (337) a Portugese neurosurgeon, published his method of carotid arteriography and by this technique demonstrated intracranial aneurysms and brain tumors. To his countryman, Reynoldo dos Santos, (128) a urologist, must go the credit for having successfully performed the first opaque visualization of the aorta (1929). Although he continued to do hundreds of translumbar aortograms with sodium iodide and thorium dioxide and concluded that the method was safe, (129) during the next decade only sporadic reports of its use, and these as a diagnostic tool in urology, came from Europe and South America. During this period various modifications in technique made their appearance. Among these were such procedures as "counter current aortography," first performed in 1910 by Castellanos and Pereiras (51); retrograde aortography by Farinas (147) in 1911; and

such other innovations as visualization of the pulmonary artery system (Moniz, Carvallio, and Lina in 1931 using the technique of Forssmann, (161) a German physiologist who inserted a ureteral catheter into his right atrium by way of an arm vein); and radiopaque angiocardiography (Castellanos, Pereiras, and Garcia (55)—1937, and Robb and Steinberg (397)—1939).

In this country, Henline and Moore (207) in 1936, using various contrast media for aortography in dogs, had a serious mortality rate which probably influenced the lack of popularity of this technique in the United States. Not until 1942, when Nelson (360) and Doss and associates (126) independently reported their successful experiences, did interest begin to be aroused. Aside from a brief halt due to World War II, progress in this field has continued unabated, (331, 410, 470) so that today practically every part of the vascular system has come under the scrutiny of contrast visualization. In addition to aortography and angiography of peripheral vessels, portal venography, splenoportography, interosseous venography, thoracic and pelvic arteriography, caval phlebography and dural sinus venography are commonplace procedures in centers of vascular surgery. Even coronary arteriography during life is possible. (206, 287) In spite of ready acceptance of many of these procedures, some concern has arisen over the number of undesirable effects that have occurred, chiefly from aortography. Many reports of fatal and near fatal complications are in the literature. Probably the most complete published analysis of this subject is that of McAffee (320) in 1957. From a survey of radiologists, urologists, and vascular surgeons in the United States, he ascertained that in 13,207 abdominal aortograms there was a mortality of 37, or 0.28 per cent, attributable to the procedure, and serious non-fatal complications in another 98 (0.74 per cent).

It is reasonable to assume that the most satisfactory contrast medium has not yet become available. With improvement in this, together with greater technical proficiency through experience, lower figures than the above could be expected. As in other techniques, so long as untrained individuals feel qualified to attempt the procedure, mortality can never be completely eliminated. We feel, as Kincaid and Davis (262) have remarked in their most thorough review of the subject, that angiography in general should only be performed when the information to be gained is essential to the management of a vascular problem and is worthy of the risk involved. With increased clinical experience, the less acute becomes the need for these procedures.

The discovery that certain impure extract of the liver inhibited the coagulation of blood was made in 1916 by McLean, (328) a student of Howell. Subsequently, Howell and Holt (223) carried out extensive investigations and named the responsible substance "heparin." Early experiments on animals and clinical use of the drug (311) were discouraging due to the toxic symptoms produced. It was not until Charles and Scott (56-58) succeeded in preparing the material in the form of a crystalline barium salt completely free of toxic properties that interest in its potential clinical value was revived. To Murray (351-353, 355) of Canada, through animal experiments begun in 1932 and subsequently accumulated clinical data, must go much of the credit for pointing out the value of this drug in vascular surgery. His results demonstrated that small vessels could be sutured with a markedly decreased incidence of thrombosis when heparin was used postoperatively for 72 hours. (Guthrie used neither local nor general anticoagulant agents, such as hirudin [leech extract] which was then available. He felt that successful results may be achieved without them.) Since then, the use of heparin for flushing the lumen of an open blood vessel during vascular repair or anastomosis and its instillation adjacent to occluding instruments is common practice by practically all who do vascular surgery. Upon less firm footing, however, is the use of heparin systemically in the immediate period following vascular replacement and anastomosis, the time during which thrombotic occlusion is most apt to occur. The risks of anticoagulant therapy at such a time need no elaboration. Most reports of patients so treated contain a great incidence of minor and even severe bleeding. In our own experience, using deep subcutaneous injections of aqueous heparin solution at intervals of four hours in individuals subjected to extensive endarterectomy of peripheral vessels has been an annoying complication.

Aside from the consideration of bleeding, a question has arisen concerning the inhibitory effect of heparin upon healing. This subject has recently been thoroughly reviewed by Deterling's group. (4) Their experimental evidence, similar to others, (114, 273, 297, 408) indicates no impairment of tensile strength or abnormality in anastomotic healing as a result of heparinization.

For a time, postoperative regional heparinization, as suggested by Murray, (355) Freeman, (165) and others, (28, 125, 485) was popular in an attempt to eliminate the disadvantages of prolongation of systemic clotting time. Because of the disadvantages attendant with maintaining a cathater in a vessel for a prolonged time; because with adequate local

effect prolongation of systemic clotting time is almost inevitable; and because it is from the operative site where most of the problems concerned with heparin arise, this procedure is today infrequently used.

It is our opinion, based upon personal experience and the published results of others, that the use of systemic anticoagulants following vascular surgery are seldom warranted if technically satisfactory suture and anastomosis have been carried out. We are particularly reluctant to use it following vascular surgery within the abdomen. The use of heparin in conjunction with extensive endarterectomy of superficial femoral and popliteal arteries would seem to be, and has been to us, worthwhile in certain instances.

The true worth in vascular surgery of dicoumarol (and its derivatives) isolated by Link (45) in 1911 as the substance in sweet clover that reduced coagulability of blood, remains to be ascertained. It would not seem unreasonable, following grafting or endarterectomy of peripheral vessels or occlusive disease, that those individuals be indefinitely administered such an anticoagulant (just as in patients with coronary artery disease). Perhaps some of the late failures and disappointing results could be eliminated.

III.

Had trauma to vessels, either acute or the late sequellae such as arteriovenous fistulae, been the only conceivable outlet for the practice of vascular surgery, it is extremely unlikely that this field would have developed as it has. For, except during and after times of war—and even not then as more esthetic means of mass execution are developed—it is unlikely that a single surgeon or group of surgeons would encounter a sufficient number of cases to stimulate the fervor of activity such as has occurred in this field in the past five years. Stimulation arose from two other sources during this period: (1) the concept of vascular surgery for segmental occlusive disease, and (2) the early successes in the management of congenital vascular abnormalities.

To René Leriche (283) of France must go the honor for having pointed out in 1923 that a segmental type of thrombotic obliteration of the vascular system occurs and that the ideal treatment of this condition would be to resect the obliterated zone and to bridge the gap with a graft. Further reports in 1940 (284) and 1948 (286) concerning the nature of this condition which has come to be known as "Leriche's syndrome," aroused further interest and pointed the way to a potentially

unlimited field of opportunity in vascular surgery, at least until such a time as when the biochemist conquers atherosclerosis.

A forerunner of what the future held in store insofar as congenital vascular defects are concerned occurred in August of 1938 when, 32 years after John Munro (350) of Boston first suggested that it could be done, Gross and Hubbard, (185) also of Boston, succeeded for the first time in ligating a patent ductus arteriosis. By 1944, Gross (182) was able to publish a report of 14 successful cases. The same year (November 29, 1944), Alfred Blalock (34) did his first successful operation for the correction of congenital pulmonary stenosis and tetralogy of Fallot, thus affording a treatment for the "blue baby." A month prior, Crafoord (76) of Stockholm succeeded in correcting a coarctation of the aorta. On July 6, 1945, Gross (183, 186) was likewise successful. Because of his continued interest in the problem and extensive laboratory investigation with the insertion of aortic homografts, (182) after resecting a coarctation in a seven-year-old boy and finding that he could not re-suture the ends of the aorta except under extreme tension, it was only logical that he insert a preserved segment of stored human aorta.

Thus, in 1949, more than four decades after Guthrie had experimentally demonstrated its feasibility, Gross (184) accomplished with success the first insertion of an arterial homograft in a human. The effects were instantaneous and astonishing. A new era in vascular surgery began. For the next decade, surgeons were to concern themselves in unprecedented fashion, both in the laboratory and in the clinic, with blood vessel grafting.

Explanation for the hiatus of almost forty years following the establishment of most of the fundamental principles of vascular surgery and for the sudden impetus to the elaboration and widespread clinical application of such surgery is a difficult task. To suggest that successful blood vessel surgery in humans could only be anticipated as a logical sequella to the development of such ancillary measures as anesthesia, blood transfusion, anticoagulants, and other previously mentioned historical milestones, is redundant and irrefutable. But it is unlikely that this is the entire reason, any more than it would be fair to attribute the lag to a deficiency in the technical skill of a prior generation of clinical surgeons.

What part that elusive factor, which might be designated as "first-ism," played in detonating this facet of surgery is difficult to assess. Why did the running of the 4-minute mile which defied attainment prior

to its accomplishment by Dr. Roger Bannister, almost immediately come so "commonplace" as to attract little interest? The insertion the blood vessel graft by Dr. Gross precipitated similar successes.

A plausible explanation is available. Following World War II th was a greater universal acceptance of the experimental laboratory as integral part of surgical training and practice. In part, this was m vated by the need to accommodate large numbers of physicians retu ing from the War who were desirous of specialty training or who w becoming reestablished in clinical practice. As a result, many you men, surgically oriented, had an opportunity to utilize their imagi tions and energies to advantage, unrestrained by the fashions of ceptor training of prior decades. Whatever the initial motivation, closer union of the laboratory with the clinic has altered permanen the surgical philosophy of this country. We believe it is to this t the resurgence and rapid development of blood vessel surgery, as scribed in the following portion of this review, might well be attribut

IV.

It at once became apparent that if the use of homografts was flourish, a suitable technique for the sterilization and storage of bl vessels was mandatory. This, of course, had been contemplated ye previously by a number of investigators. Carrel (48, 49, 52) repor blood vessel preservation by refrigeration above freezing in such me as salt solution, humid air, defibrinated blood, vaseline, glycerine, other materials. Although his results and conclusions are based few animals, making it difficult to evaluate them, others (36, 443, 4 of that period reported similar findings using a variety of soluti (Locke's, Ringer's, etc.).

Following the reports of Gross, Hurwitt, Bill, and Peirce (184, 1 favoring the balanced salt solution of Hanks for the storage of ves at 1 to 4° C., renewed interest in such a means of preservation generated. This group (380) demonstrated that vessels so maintai for as long as 37 days remained viable in tissue culture, as determi by fibroblastic proliferation, and that a substantial number stored as long as 30 days had normal silver staining of the epithelum. (3 Subsequently, workers both in this country (62, 334, 445) and Europe (91, 92, 211, 279, 369) substantiated the findings of Gross associates. Some, (404) however, felt that the addition of homolog serum to the balanced electrolyte solution gave better results; ot preferred blood and citric acid (10), citrated blood and dextrose (

475), the addition of cortisone to the salt solution (319), and other minor variations of the storage media. As Lehr and Blakemore (281) have concluded in their comprehensive review of this subject, it would seem that balanced salt solution containing antibiotics, with or without the addition of nutrients such as blood or serum, affords a highly satisfactory medium for several weeks' storage of blood vessels at temperatures of 1 to 4° C.

Although great interest by almost all investigators was centered about the length of time vessels so preserved remained viable, it soon became apparent with this and other methods of storage that it was of little moment whether grafts were dead or not, but that the avoidance of autolytic processes was the chief concern. Hamblin and Lord (194) have reported the rupture 8 days postoperatively of a homograft preserved for 76 days by Gross' (184) method. This graft had undergone histologic change during its long storage period. Indeed, Guthrie realized that there was no advantage to the use of a living vessel and rejected Carrel's supposition that they survived following insertion. Guthrie concluded that "the elements of such engrafted segments to meet the vascular requirements need not, and probably do not survive, but for a time they may mechanically perform the circulatory function and serve as a bridge for the ingrowth of other cells, and themselves ultimately suffer degenerative, disintegrative, and absorptive changes." In fact, there is evidence that the insertion of non-viable homografts is preferable in that they produce less of a cellular reaction by the host. (154, 267, 376)

With increasing demands for vessels and the birth of the concept of vessel banks, it was apparent that methods of more enduring preservation and allowing for more convenient transportability were imperative. Thus it was that the technique of quick freezing and storage at about −70° C., as reported by Hufnagel, (136, 226) acquired advocates. (109, 159) By this method. Deterling and associates (121) maintained grafts for eight months with good results.

At about the same time (1949), Peirce, Rheinlander, Moritz, Gross, and Merrill (381) revived the use of formalin preservation as originally described by Guthrie in 1908. (190) Guthrie had used 2½ per cent formalin and washed the graft before use in dilute ammonia, dehydrated it in absolute alcohol, and impregnated it with paraffine oil. He reported (265) that using this process a segment of abdominal vena cava interposed between a dog's carotid artery in 1908 functioned well until 1919, when the dog died of "old age." Peirce and associates,

however, reported extensive degeneration of the media and fragmentation of elastic fibers with calcification using 4 per cent neutral formalin. Although Shumacker and associates (430) did not favor formalin-fixed grafts, others (16, 279, 336) reported excellent results in dogs.

Through the years, both alcohol (92, 342, 358, 375) and glycerin (465, 466) have also been used as preservatives for animal and human grafts, and although the number of reports are few in comparison to the other methods, the results are sufficiently encouraging to suggest further evaluation.

The method of preservation of homografts which has attracted the attention of most people concerned and which has become the most universally accepted is that of freeze drying, as originally described in 1951 by Marrangoni and Cecchini (309) and by Hyatt, Turner, and Bassett. (233) Flosdorf and Mudd (156) in 1934 had applied this principle to the preservation of certain biological materials. By this method grafts are quickly frozen by plunging their containers into one of a variety of suggested coolants, such as liquid nitrogen, acetone and dry ice, trichlorethylene and dry ice, or alcohol and dry ice. Frozen to approximately −70° C., they are placed in a vacuum system which, by the process of sublimation, removes the water content of the tissue. They may be stored indefinitely at room temperature and are readily transportable. Practically every surgical unit which has so processed vessels has added their own refinements and modifications and many have published their techniques and results. (83, 135, 150, 193, 248, 281, 282, 326, 393, 394, 415)

Simultaneous with the development of a means of blood vessel preservation, it was urgent that suitable methods for their sterilization be obtained. *Unfortunately, since freeze drying does not routinely kill all* microorganisms, it is necessary to sterilize the blood vessels before lyophilization. The original process, as described by Gross, of removing tissue at autopsy using sterile surgical technique was not always feasible. Frequently vessels thought to be taken aseptically were found on culture to be contaminated. Obviously, the method of sterilization had to be practical and could not be injurious to either the blood vessel or personnel. In 1951, Meeker and Gross (330) reported the sterilization of frozen grafts by subjecting them to high voltage, cathode-ray irradiation. They were of the opinion that 2.0 to 2.5 million roentgen equivalent physical units (R.E.P.) gave the best results and that above 3.0 million R.E.P. severe and irreparable changes to the graft wall occurred. Hammer, (195) on the other hand, subjected lyophilized

grafts to a dosage of 4.0 million R.E.P. and reported adequate sterilization and no tissue damage. Hui and associates (230) found that grafts irradiated with a 1.6 million R.E.P. revealed marked degenerative changes and heavy calcification two months after implantation. Others (42, 267) found no such changes.

Thus it would seem that lack of availability, cost, need for special equipment and disagreement as to proper safe dosage have prevented the general acceptance of this method.

Ethylene oxide sterilization, as has been proposed by Hufnagel (229) and by Creech, (83) although used apparently with success, (162) has several disadvantages. It is highly explosive; freeze drying must be instituted at once after removal of the ethylene oxide or vessels tend to become tough and inelastic; and it has been found that in grafts so treated the elastic lamellae were disturbed so that the grafts developed aneurysmal dilatation. (426) From a recent disconcerting report by Cockett and Norman, (60) there is reason to believe that such a surface sterilizant does not reach bacteria already spread within the vasa-vasorum of the graft.

In 1954, investigators (298, 452, 459) of the Henry Ford Hospital in Detroit obtained good results using beta-propiolactone as a sterilizing agent. Its value depends upon meticulous adherence to technique with proper buffering and incubation. Like ethylene oxide, this technique does not protect the graft from contamination during its further processing. Also, it may have an adverse effect upon the subsequent fate of the vessel after grafting. A recent report by Sutherland and associates (444) indicates that beta-propiolactone is superior to ethylene oxide as a sterilizing agent; it has greater sterilizing powers and is much easier and safer to use.

Other methods of sterilization suggested were those of Mortensen (346) using merthiolate solution to maintain sterility of grafts maintained in nutrient medium, and of Ross (401) who immersed grafts in formalin for eighteen hours and then, following washing, preserved them by either freezing or freeze-drying.

In seeking better methods, we (150) reported that simply treating contaminated vessels with massive doses of antibiotics for several days prior to lyophilization was adequate for sterilization. Utilizing this technique in our own vessel bank, we have used several hundred grafts in animals and humans over the past few years with satisfactory results. Confirmation of the value of this technique has been obtained. (306, 457)

late, it is difficult to state with assurance which methods of preser- and storage of vessels are the best. Unfortunately, popularity frequently bears the connotation of excellence. Nowhere is this rue than in the clinical practice of surgery. It would seem that ›st popular method of handling homografts is to chemically treat vith either ethylene oxide or beta-propiolactone and to lyophilize It is annoying that not one experiment has been reported in grafts after various types of preservation and sterilization have roperly evaluated and compared under controlled conditions for racted period of time following insertion.

V.

comitant with the preceding studies countless investigators were ting various facets of blood vessel grafting in both animals and ıs. In fact, it has been facetiously commented that almost every on who had a dog and a resident at his disposal began an investi-.. Unfortunately, on occasion impatience led to human applica- efore the results in animals were completed. Most of the work rned itself with (1) the fate of the homograft, (2) improvements gical technique, or (3) clinical application.

ieral agreement exists that fresh arterial autografts survive as structures with either no change or only intimal thickening.

t as Klotz, Permar, and Guthrie (265) indicated in 1923, recent igators (1, 63, 179, 259, 291, 334, 365, 410, 445) have reported ll homologous vascular grafts, whether fresh or preserved (by any s), eventually lose their cellular integrity. Such grafts are sooner er converted into fibrous tissue tubes by the ingrowth of host ctive tissue cells. Loss of smooth muscle fibers of the media, cement of the intima and adventitia of the graft by fibrous con- ve tissue derived from the host, and calcification are consistent ıgs.

hough the elastic lamina may still be present when much of the of the graft is no longer distinguishable, as time goes on this be- s more fragmented and less conspicuous. The degree of calcifi- n observed seems in some way related to the method of preserva- of the graft. It was extremely prominent after the use of formalin,) and was conspicuous in grafts preserved in light mineral oil nineteen days after implantation. (365) Further, greater involve- occurred in grafts of the thoracic aorta than in the abdominal . (256) Similar deposits were observed by Coleman and asso-

ciates (63) in quick-frozen and in nutrient-preserved grafts in dogs four years following transplantation. To be sure, calcification not infrequently occurs in human arteriosclerosis, but the degenerative changes referred to by the various authors are most reminiscent of a non-specific reaction to devitalized tissue of the Mönkeberg type of arteriosclerosis, rather than that seen in the atheromatous form of human arteriosclerosis characterized by intimal lipid deposits, as well as fibrosis and occasional calcification.

In this connection, it was of interest to know whether homografts would be prone to develop arteriosclerotic changes seen in the host vessels. Our own results with induced cholesterol arteriosclerosis in rabbits (155) demonstrated a marked susceptibility to atherosclerosis in both fresh and lyophilized aortic grafts, but more so in the former. Similar results were found by Creech and associates (87) in dogs, and Rustad, Gregg, and Prior (405) in rabbits. DeBakey, (106) however, in the first comprehensive report of structural changes occurring in aortic homografts in humans was explicit in reporting that although all of the other changes seen in animals occurred, no atherosclerosis or calcification was noted in one graft retrieved 360 days after implantation. A subsequent report by his group (82) on the fate of aortic homografts in humans from 1 to 2½ years after transplantation emphasizes the fact that much of the structural pattern of the graft is retained while it is being reinforced by fibrous connective tissue of the host. An observation by Haimovici (192) worthy of note was the finding that fresh thoracic aortic implants into abdominal aorta showed far less susceptibility to atherosclerosis than did the host abdominal aorta. It is suggested that, in view of the difference of these findings from those of Creech and ourselves, there exists a biologic difference between the two aortic segments.

One interesting controversy that arose concerned the origin of the new intima seen in homografts. It was at first felt that this occurred as a gradual ingrowth from the host intima at the two ends. Best opinion at present is that what appears as intima is in reality a layer of fibroblasts which have become so flattened as to be practically indistinguishable from the host intima. In what is probably the most thorough study of this problem, Poole, Sanders, and Florey (383) concluded that new endothelial cells are formed by mitotic division from preexisting endothelial cells and that there is no evidence that endothelium comes from any other tissue or that there is anything unusual about the mode of nuclear division. However, it would seem that when large

segments of vessel are denuded of endothelium or arterial homografts are inserted, (393) while endothelium will begin to regenerate from either end, even after protracted periods of time (seven months) (383) it will still not completely cover the defect.

Although observations have been made on the lining that develops within synthetic grafts, there is no agreement as to its origin. As Poole and associates point out, many authors have used the word "endothelium" to mean the inner lining of cells without implying that it originates from or is identical with normal endothelium.

Because of the necessity to insert grafts into children, the question naturally arose as to whether or not the lines of anastomoses would grow with the child and whether free blood vessel grafts would increase in size with the growth of the host. This problem concerned numerous groups of investigators. Johnson, Kirby, Allam, and Hagan (241, 242) demonstrated that the use of continuous posterior and interrupted anterior silk suture did not significantly limit the growth of vascular anastomoses in pigs. Also, the growth of vena cava and aorta autografts in pigs equalled that of the aorta in which the grafts were placed. The growth of homografts was equally as good. Others (172, 407) found that if a continuous suture of silk were used, the growth of anastomoses was impaired, but that if the sutures were interrupted (411, 412, 430) or of catgut, (411, 412) no constriction occurs. In another study by the Harkins group (364) at the University of Washington, it was found that some enlargement of grafts can take place, but, as a generality, thoracic aortic homografts tend to lag behind the host aorta. This was irrespective of the graft length or of duration of preservation.

Thus it would seem that vascular anastomoses in children should be performed using a semi-interrupted silk suture, and that if homologous tissue is used for grafting, some discrepancy in size between the graft and host might be anticipated. The consequence of the latter has yet to be reported.

Another point of interest was if and how arterial homografts become revascularized. Studies by McCune and associates (324) and Kiehn, *et al.*, (260) have confirmed the assumption that the free vascular graft obtains its blood supply from the host by the ingrowth of vessels through the adventitia. The former group demonstrated this by India ink injections and by wrapping the arterial graft in cellophane®. Under such conditions no vascular channels could be observed coming from the lumen. They did concede that the inner layers could be nourished

by diffusion from the lumen. The latter workers concluded the same thing by functional methods, i.e., the graft uptake of P^{32}. Further, Bencini and Bellinazzo (16) demonstrated that if arterial grafts were wrapped with polyethylene, the outer layers of such grafts became necrotic. These findings gave credence to the idea that it is proper to cover the implanted graft with surrounding connective tissue to facilitate revascularization. (15)

Insofar as the technical aspects of blood vessel suture and anastomosis are concerned, the fundamentals were firmly established by World War I. The contributions of Guthrie during the first decade of this century are monumental. Through the years, reiteration of these principles by numerous authors (220, 254, 359, 423) have been published and attempts at introduction of slight variations have been made. (174) But, the methods of suture either continuous everting, over and over, or interrupted are essentially as originally described. Types of suture material have varied, but in general make little difference in the end results. (382) The effects of arterial clamps on vessel walls have been investigated by Henson and Rob. (209) They found rubber covered bulldog clamps, tape tourniquet, or Crile clamps the least traumatic, while those clamps which are the most popular (Blalock, Crawford, Brock, Potts) produced considerable trauma to the vessel wall. Wehn (474) has advocated, based upon certain anatomical and physical studies, that whenever possible, direct transverse incisions should be used for arteriotomy rather than the axial incision which is most frequently used.

In recent years there has been rejuvenated interest in non-suture techniques for blood vessel anastomosis. Many of these are in principle similar to those described by Guthrie. The contributions of Blakemore and Lord (30, 31) using vein lined vitallum tubes, Weiss and Lam (476) vein lined tantalum tubes, Swenson and Gross (447) absorbable fibrin tubes, Egdahl and Hume (143) polyethylene tubes lined with autogenous vein, have all failed to attain practical clinical importance. Much interest in this country has been generated by the Russian invention of an apparatus capable of joining together the ends of vessels with metal clips. (2) Other blood vessel anastomosing machines have been described by Tibbs (458) of England, Inokuchi (234) of Japan, and Vogelfanger and Beattie (467) of Canada. We have had the opportunity to personally observe the Russian and English devices and are convinced that they have an important place in the experimental surgical laboratory, but that their clinical application is

extremely limited. At present there are no non-suture techniques recommendable for clinical use.

As more and more such fundamental information was accumulating, the greater became the number of reports concerning the clinical use of *homografts.* Shortly after DuBost, Allary, and Oeconomos (130, 131) described the first successful resection of an abdominal aortic aneurysm and insertion of a homograft, DeBakey and Cooley, (99) in a series of articles, began to report what certainly is the world's most extensive experiences with excision of aortic aneurysm, both abdominal (99) and thoracic. (67-69, 98) No segment of aorta escaped them. Among their illustrious accomplishments were the resection of the entire ascending aorta for fusiform aneurysm, (70) total excision of the aortic arch for aneurysm, (73, 84, 102) and excision and replacement by homograft of a segment of lower thoracic and proximal abdominal aorta harboring an aneurysm, (72, 107) using in all some form of bypass or controlled extracorporeal circulation. Others are now duplicating their successes. Schimert's group (418) has repaired an aneurysm of the aortic arch; Etheredge and colleagues, (146) Davis and associates, (95) and Hurwitt (232) have recorded the resection of aneurysms involving the celiac axis.

To Bahnson (5-7) must go credit for having first successfully excised a leutic saccular aneurysm of the ascending aorta following clamping of the neck of the sac and for, in general, contributing to the surgery of aortic aneurysm. Robb, (395) Wheelock and Shaw, (480) Szalagyi, (454) Lam, (271) and others might well be considered pioneers in the surgery of aortic aneurysm. Led by DeBakey, (97, 100) who first reported operative success in the treatment of dissecting aneurysm by creating a distal internal opening as a re-entry site with closure of the distal aneurysmal space, Warren, (473) Swann, (466) and others have described success in the management of what was formerly a uniformly fatal catastrophy. Gerbode (170) has successfully handled traumatic thoracic aneurysm in three of four individuals by resection and grafting. An increasingly large number of successes in the management of *ruptured aortic aneurysm* have been reported (148, 198, 239, 304, 322, 434) since the publications of Cooley and DeBakey (five cases with a 40 per cent survival in 1954), Bahnson, (6) and Gerbode. (169) By 1956, Cooley, DeBakey, and Creech (71) were able to present twenty-five cases with a 64 per cent survival. The latter figure, we are sure, by no consideration represents the general experience in this country. While this is difficult to assess because human nature precludes reporting

failures, it would not be unreasonable—and even then a bit optimistic—to estimate a 35 per cent success rate. No embarrassment or shame need be felt about this when it is realized that but a few years ago the mortality for ruptured aneurysm was virtually 100 per cent.

Because of the magnificent advances in surgery for aneurysm, particularly of the abdominal aorta, and because of the statistical findings of Estes, (145) Scott, (421) and Wright (484) that, if an aneurysm is found by chance examination with only minor or no symptoms, 30 to 40 per cent of such patients would be dead within one year, it would seem that resection and grafting are the only and immediate procedures of choice. This is even more mandatory if symptoms are present, for the analyses of Kampmeier (255) and of Gliedman (173) showed 80 to 90 per cent of patients dead in less than one year.

Surgery for occlusive disease of the aorta and major vessels is of three types: (1) excision with graft replacement, (2) by-pass grafting, and (3) endarterectomy. Oudot (370-372) in 1951 and in 1953 reported successful resection of the aortic bifurcation and replacement with a homograft. Julian (253) in 1953, DeBakey (105) in 1954, and Szilagyi (451) in 1955 were among the first in this country to record their experiences with this method of management of aorto-iliac occlusion. Based upon short term follow-ups, approximately 80 pe[r] cent of their results were good and they lent encouragement to suc[h] management in this type of segmental occlusive disease.

More recently, Welch, Kirklin, Ellis, and Bruwer (477) reported the experience at the Mayo Clinic with 99 patients on whom resection and homografting (Ivalon used in 2) for chronic occlusion of the aorta or iliac arteries was performed. Seventy-one had an excellent result, 15 a fair result, and 5 died as a consequence of the operation. The Cleveland Clinic experiences were recorded by Humphries, deWolfe, and LeFevre. (231) They classified their patients as being "good" candidates for surgery if they had segmental blocks with claudication only, and in this group resection and homografting were successful in 92 per cent of 88 cases. In a "poor risk group" having minimal exit flow of blood and marked rest pain, rubor, gangrene, and prolonged venous filling time, there were 60 per cent favorable results in 20 patients. In September, 1958, DeBakey and associates (103) recapitulated their experiences with 173 cases of aorto-iliac occlusion treated by homograft replacement. Ninety-two per cent was classified as successful, and the mortality rate was only 4 per cent.

Simultaneous with the development of the use of homografts for aorto-iliac occlusive disease, *treatment of arteriosclerotic* occlusive disease of the lower extremities was attracting attention. Rob (396) and Julian (252) favored resection of the involved vessel and insertion of an autograft or homograft by end-to-end anastomosis. Others (77, 118, 296, 451) *were utilizing this technique in their earlier experiences.* Cockett, (59) however, because of the high incidence of thrombosis and stenosis at the site of anastomoses, utilized an arterial homograft as a by-pass. This was fashioned after the technique of Kunlin (270) who *inserted* a *venous graft as* a *parallel* shunt with end-to-end anastomoses. He thus preserved the collateral branches and the main arterial channels. At once this technique became popular. The rationale of transporting the flow of blood around a block while avoiding operative trauma, *interference* with collaterials and damage to concomitant veins was appealing. Shaw and Wheelock, (427) Linton and Menendez, (296) Crawford and DeBakey, (77-79, 104) and others (64, 118, 224, 274, 377) were quick to utilize it and report their experiences. Linton (296) in 1955 recorded that of 20 arterial homografts inserted by end-to-end anastomosis, 12, or 60 per cent, failed in 6 months and only 8, or 40 per cent, functioned after 8 to 20 months. With the by-pass technique, however, *in 16 instances 3 failed due to sepsis, and 81 per cent* functioned for one to 8 months. In DeBakey's earlier experience, (77) 10 of 12 femoral arteries were managed successfully by excision and graft replacement and by-pass was effective in 21 or 24 occluded femoral arteries. These cases were observed from 6 months to less than 2 years. More recently, he and his colleagues (104) reported 87 per cent patent grafts in 54 femoral by-passes with the longest follow-up of 2½ years, and in another publication in 1958, (80) 85 per cent initial success in 83 homografts for femoro-popliteal occlusion. Failure of grafts occurred 3 weeks to 38 months in 13 (18 per cent) of homografts, and 7 of these were successfully regrafted. Similarly, Payne, Rudy, and Winsor (377) *reported glowing results with short follow-up.* Of 23 extremities treated with by-pass graft technique, initial results were excellent in 17, improved in 2, and poor in 4. Deterling, (118) in a two-year follow-up, reported an 80 per cent success for 39 femoral homograft by-passes.

These successes are not to be construed as universal, for Laufman (274) has reported a 42 per cent failure rate in cases followed 6 to 10 months; Hoye and Warren (224) had none of 5 by-passes remain patent more than one year; and Szilagyi (456) had 48 per cent of his

femoral popliteal by-pass homografts close by 33 months. As a matter of fact, the latter author reported that of 120 homografts inserted for peripheral arterial disease and followed one to 33 months, 19 per cent occluded immediately postoperatively and 20 per cent more subsequently lost function. He was of the opinion that the failure was due to the extent and severity of the pre-existing arterial disease, either through postoperative progression or owing to incomplete excision. Although failure could be traced to intrinsic defects in the graft only in rare instances, 17 per cent showed progressive angiographic changes which might in time lead to occlusion. Warren (471) was of the opinion that the 70 per cent closures in by-pass grafts seen by him were largely the fault of degenerative changes occurring in the homograft rather than progression of the patient's disease. In a more recen analysis of his experiences, Szilagyi (450) was more pessimistic about the eventual fate of homografts. He felt that their future was poor, and though perhaps the bulk of aortic grafts will remain free of change for about 5 years, it is then that they will begin to endanger life. For femoral grafts the forecast was less favorable. He anticipated only one-third of such grafts to be in a safe and functional state at 3 years, and that by 5 years there was but little chance of function. By 1958, Linton (293) tempered his prior enthusiasm by noting that of 38 patients with by-pass arterial grafts followed for 2 to 3 years, only 60 per cent were still patent.

So, whether the gradually increasing number of failures that occur following homografting as the years progress is due to graft failure or "patient failure" remains to be clarified. It is not unreasonable from the evidence available to implicate both. What truly is a discordant note is the ever-enlarging number of reports of homograft ruptures (37, 118, 139, 149, 166, 194, 329) and/or aneurysmal dilitations (112, 191, 238) following insertion in humans. But then, of course, all of this might well have been expected from results in animals for, in the human, as in the dog, it has been demonstrated (450) that there is eventual loss of all tissue elements except the elastic fibers with connective tissue ingrowth of variable extent into the adventitia and outer media. A pseudointima is formed, and as the age of the graft progresses the elastic fibers become fragmented, diminished in number, and the grafts become weakened.

In 1953, Brock (37) summarized the philosophy of clinical vascular grafts at that time, when he said: "... the achievements with homografting are sufficiently numerous and sufficiently encouraging to justify con-

tinuance, even though the later follow-up may reveal disadvantages and disappointments. . . . The patients have certainly gained a great immediate advantage."

In 1959 we do know that homografts are less than ideal and, in fact, somewhat disappointing. Should they be abandoned? This depends entirely upon whether there is a substitute that will promise better results. Let us review the information available concerning the use of other blood vessel replacements and then attempt to answer this question. //

Even before their true value could be ascertained, it readily became apparent that the supply of arterial homografts was inadequate to meet the needs of this expanding field of surgery. When an inventory was made of the body's own tissues which might be expendable and utilizable for bridging vascular defects, segments of autogenous vein offered a possibility. Had not Klotz, Permar, and Guthrie (265) in 1923 suggested their value based upon Guthrie's prior experimental results? *Indeed, Bernheim (21) in 1916 reported the first successful case in the* American literature when he used a vein graft to bridge a defect in the popliteal artery following excision of a leutic aneurysm. Shumacker (428) in 1948 reported the replacement of arterial defects in 6 patients with saphenous vein autografts who were followed 5 weeks to 4 months with excellent results in 5 of the 6. Schloss and Shumacker (419) in 1950 compiled a comprehensive historical review of the earlier use of venous autografts with particular reference to histological observations. Although there was difference of opinion regarding the nature and degree of structural change, all investigators concluded that venous autografts persisted as living structures but underwent histologic changes chiefly in the nature of fibrous reinforcement. It was felt that these alterations were most likely the result of the arterial pressure. In a subsequent study by this group, (435) it was reported, based upon a follow-up of less than 10 months, that fresh venous autografts and homografts, venous homografts preserved by freezing, and homo and heterografts previously fixed in formalin, are all capable of functioning effectively to bridge defects in the thoracic aorta, but that only the fresh autogenous graft survives as a living structure, and all but this type appeared microscopically to undergo destruction. These and a few other early reports (243) suggested that the use of venous autografts might hold promise, particularly if they were used in the extremities (65, 362, 412) where muscular support was available. For it soon became evident that unsupported fresh venous autografts placed in the

thoracic aorta of both the growing pig and dog underwent considerable dilatation (244, 257, 268, 406, 413) in a relatively short time. Similarly, this was seen in the abdominal aorta of dogs by Nabatoff, Touroff, and Gross. (357)

To prevent this undesirable sequella, a multitude of techniques have been described. Vein grafts have been wrapped with skin, (124, 406) fascia lata, (406) pericardium, (244) nylon mesh, (464) viable intercostal muscle, (366) tantalum gauze, (441) and plastic sponge. (344, 441) Dicetylphosphate has been applied to the surface of venous autografts. (257, 492) While some of these have been encouraging, none has been entirely satisfactory. More recently a method of venous plication has been described by Nyhus and Harkins (363) which has decreased the incidence of early graft thrombosis (420) by eliminating the disproportion between the diameter of the graft and recipient aorta. However, prevention of subsequent dilatation has not been accomplished. It may thus be concluded that the use of autogenous veins in the aorta, iliacs, and other major abdominal arteries has no clinical application at the present time. Aside from the difficulty in obtaining a segment of adequate size, experimental evidence has demonstrated that thrombosis and aneurysmal dilatation are universal.

The use of autogenous vein grafts in the extremities, particularly for the femoral artery, is another story. First reports by those using this type of graft for obliterative disease were discouraging. Fontaine (157, 160) reported only 5 of 25 such grafts patent after one year with but 12 patent one month after surgery. Similar subsequent failures were described by Malan, (308) Eastcott, (134) and Dye, Grove, Olwin, and Julian. (132) The latter group had an initial failure rate of 50 per cent of 30 such cases. (133) They ascribed their late failures to improper selection of cases or inadequate resection of obstructed segments rather than to fault of the vein graft itself. (132) The results of Lord and Stone (300) emphasize this point. Twelve venous autografts inserted in extremities for arterial injury, arteriovenous fistula, or malignancy remained functioning for as long as 7 years with no evidence of aneurysmal dilatation or degeneration. On the other hand, utilizing the by-pass principle in 8 cases for obliterative disease, success was achieved in only 4 instances. They, likewise, attributed the failures to the disease itself and not to an inherent deficiency in the graft.

Others, too, have had excellent results where venous autografts were used for other than arteriosclerosis. Murray (354) reported a 15-year follow-up of such a graft inserted for trauma. No evidence of aneurysm

or calcification was present. Jahnke and Seeley (237) stated a definite preference for them in immediate reconstructive procedures upon the peripheral arteries.

Arterial homografts for obliterative disease were more successful than venous autografts in the experience of Shaw and Wheelock, (427) as they were for Deterling (116) (1957) who observed a "high percentage of thrombosis of long vein grafts used in occlusive disease of the extremities." Similarly, Hoye and Warren (224) (1956) reported closure within a few months in 8 of 13 venous autografts inserted into the arterial system of the lower extremity using both end-to-end and by-pass techniques.

Recently (1958-1959), several reports have suggested that there still exists a future for this type of graft. Linton (294) has unequivocally placed saphenous vein autograft, put in by end-to-side by-pass technique, as his first choice for treatment of obliterative disease of the femoral artery. Experimental and clinical data of Jones and Dale, (245) Dale, DeWesse, and Scott (90) and Dale and Niguidula (89) are encouraging. These workers (245) have presented evidence to suggest that the lack of dilatation of the veins when placed in the extremity in contrast to the aorta or iliac arteries might be due to lesser tension on the wall of such veins because the radius is so much smaller (Laplace Law; Tension = Pressure X Radius), rather than to the external support afforded these vessels.

Thus, although at this writing one can detect a slight resurgence of interest in by-pass autogenous vein grafts in obliterative disease of the extremities, there are no unequivocal data to support their use. In fact, there is much to suggest that they are less than satisfactory. However, in contrast to homografts, it would seem that the failures have been due to progression of the patient's disease rather than because of deterioration of the graft. At the risk of belaboring a well-worn vascular surgical cliché, "more time and data are needed for their proper evaluation." The clinical use and worth of autogenous vein grafts to bridge arterial defects in the extremities due to causes other than atherosclerosis where the vascular "run-off" is through normal vessels, seems to be more firmly established and confirms the early experimental findings of Guthrie.

Venous homografts, because of their difficulty in procurement, problems in processing, and production of an undesirable host response, have no advocates.

Although Guthrie (53) and many others concerned themselves with the transplant of a free segment of vein into an artery, little concern until recently has been engendered as to what might best be inserted into the venous system as a graft. That there is real clinical need for this knowledge is apparent from the occasional report of superior vena-caval syndrome which might have benefited from surgical intervention and in radical cancer surgery where replacement of a segment of inferior vena-cava, portal or femoral vein has been indicated. While various plastics such as tubes of ivalon sponge, (119) nylon, (43, 119, 416) dacron, (119) orlon, (43, 144) lucite, (94) teflon, (43, 94) and polyethylene, (144) were tried, no enduring success has been achieved with their use. Aortic homografts (35, 43, 96, 119, 196, 212) have been used both clinically and experimentally with slightly better success and are by no means satisfactory. Kay (258) achieved success in only 30 per cent of dogs in which he inserted caval homografts, while Bryant and associates (43) and Schauble and colleagues (416) had no success. Apparently only autogenous vein grafts afford worthwhile results, (43, 264, 403, 416) and these, too, may fail when compiled from smaller veins. (3) The problem of obtaining adequate autogenous tissue would seem to be a limiting factor in solving this problem at present. However, Moore (341) has suggested that since segments of aorta may be satisfactorily replaced by prostheses, these should be removed and used for superior vena caval replacement. Obviously, more work must be aimed toward the development of an adequate prosthesis for the venous vascular system.

Concomitant with the evaluation of arterial homografts and venous autografts, interest in vascular heterografts was rejuvenated. Guthrie (189) in 1907 was one of the first to achieve functional success with such grafts when he reported that a fresh segment of cat's aorta transplanted between the ends of the divided common carotid artery of a dog was functioning after 51 days, and a segment of rabbit's aorta similarly placed showed good results at the end of 31 days. He did emphasize that, although such grafts will carry blood for a time, they undergo extensive gross and microscopic change, the latter being characterized by loss of muscle cells and elastic fibers with replacement by dense, hyalinized connective tissues, calcification and osteogenesis. The historical review by Schloss and Shumacker (419) in 1949 of further studies with such grafts confirm these findings.

With this background, Hufnagel (229) in 1953 revived interest in this country with their use by reporting that aortic heterografts in dogs

functioned well for as long as 402 days, and that these segments exhibited little evidence of thrombosis or rupture. Encouraged by this, he inserted calf and pig heterografts into humans with an immediate result that was excellent. To our knowledge, no further report concerning these patients has been made. Oudot (368) in 1949 reported the implantation of heterologous arteries in human subjects, and other European investigators (168, 280, 367, 409) described their experiences. Similarly, a preliminary report by Pate and associates (376) indicated that freeze-dried heterografts were clinically satisfactory at 5 months. Kimoto and colleagues (261) were so pleased with alcohol preserved heterografts placed in dogs that they inserted heterografts obtained from dog and sheep in 5 human cases with good immediate results in all. On the other hand, a mass of evidence has been accumulated demonstrating that arterial heterografts undergo rapid destruction characterized by aneurysm, rupture, and thrombosis. Creech and associates (85) found this to be true using hog, sheep, and calf arterial segments in the aortic tree of dogs and in one clinical case where hog's artery was used to bridge a defect in an external iliac artery. Similarly, these were the findings of Lazzarini (276) implanting human arteries into dogs, Deterling (117) using goat, monkey, human, leparine, and feline vessels into the arterial system of dogs, and Sauvage and Wesolowski (414) grafting arteries of dog and man into pig and pig and man into dog. The latter workers (479) found no improvement with either fresh or ethylene-oxide freeze-dried grafts, and the site of implant (thoracic or abdominal aorta) made no difference. Other investigators (208, 347, 432, 463) have had similar experience.

In an attempt to permit better tolerance to heterografts by the host while yet maintaining their effectiveness as arterial substitutes, they have been subjected to controlled enzymatic action to remove their immunologically reactive protein. (398) A tubular bovine prosthesis of collagen resulted. In a 2-year follow-up of such grafts implanted into the abdominal aorta of dogs, Rosenberg and associates (399, 400) reported that their objective was obtained. They did alter the host response to such grafts and the percentage of success compared favorably with other vascular substitutes. They also demonstrated that perhaps the elastica offers little to the strength of a graft and that it is the collagen which is highly resistant to mechanical stress. Newton and associates (361) used horse carotids altered by peptic digestion and found a high incidence of aneurysmal dilatation.

The true significance and value of such studies remain to be ascertained. Perhaps better techniques for altering the antigenicity of the heterograft without weakening it will make such grafts clinically valuable. At the present time, only under the direst of circumstances are heterografts worthy of permanent implantation into the arterial system of humans.

VI.

Non-biological foreign material of various sorts had been inserted into the vascular system of animals and man in the past with little success. Carrel (50, 51) used glass and aluminum tubes lined with paraffin; Tuffier (460, 461) paraffin coated silver tubes in World War 1; Murray and Janes (356) glass tubes with systemic heparin; Blakemore, Lord, and Stefko (32) vitallum tubes; Donovan (125) and Moore (340) polyethylene tubing; and Hufnagel (225) methylmethacrylate. More recently, based upon the experiments of Grindlay and Waugh (181) in 1951, Shumway and associates, (17, 436, 437) Mortensen and Grindlay, (345) and others (3, 240, 310, 323, 374) reported the use of plastic blood vessels made of polyvinyl formalinized sponge (ivalon). Although early animal experiments were encouraging, thrombosis disruption or dilatation have been reported by some in their clinical (81, 290) and experimental (115, 310, 478) use. Others (3, 17, 323) concluded that poor results with this material are due to poor case selection, and that ivalon is satisfactory when used for grafting vessels the size of the common iliac or aorta in man, but not for smaller arteries. It may be concluded that the worth of this material for blood vessel grafting is not adequately proven and that until such a time it must remain low on the list of choices of materials to be used to replace blood vessels.

That no dearth of ideas exists as to what might be tried as a blood vessel substitute is evident from the recent reports of the use of siliconized rubber, (142) steel mesh tubes (26, 272) and dermal heterografts (leather). (263) In fact, the latter workers felt that, from preliminary results, further observations with the use of chamois which they defined as "leather from pickled sheepskin fleshers by tanning with cod liver oil," appeared warranted! As yet, to our knowledge, nobody has accepted the challenge.

In search of a material that was readily available without the disadvantages of procurement, sterility, preservation, and reactivity of homologous vessels, we (151) evaluated in our laboratory the use of autogenous skin tubes for blood vessel replacement. Since it was felt

at the time that the superiority of homologous blood vessels over synthetic materials was due to the presence of elastic tissue in the former, skin which contains elastic fibers might possibly be superior to other autologous tissues. Using various techniques, it was found that in all, aneurysmal dilatation, distortion and histologic changes were so great as to make it seem undesirable to use such tissue to replace defects in the human aorta.

Perhaps the only completely new concept in vascular surgery to arise in this decade (after 1950) has been the utilization of synthetic fabrics for blood vessels. Voorhees, (115) while inserting valve leaflets in dog hearts, noted that silk thread lying free in the beating right ventricle of the dog rapidly became endothelialized. As a result of this observation, it was conceived that prostheses of fine mesh cloth might be used to bridge arterial defects. Consequently, in 1951, porous vinyon N tubes, prepared by folding such cloth and stitching it longitudinally, were inserted into the abdominal aortas of 15 dogs. Results of these studies reported by Voorhees, Jaretzki, and Blakemore (469) were extremely encouraging. By the spring of 1953, based upon a 2½ year experimental study of such grafts, this group began to use cloth prostheses clinically, and in 1954 they reported 18 cases of arteriosclerotic aneurysm treated by resection and implantation of cloth tubes. (33) They were gratified by the versatility of the grafts and the functional results obtained.

At once, the fancy of vascular surgeons became titilated by the prospects of something as prosaic as "yard goods" serving as blood vessel substitutes. Assembly-line insertion of grafts of a variety of fabrics began in earnest. A new vocabulary and an understanding of the textile industry were rapidly acquired by the more zealous. Words, such as cloth porosity, denier, taffeta weave, calendering, and crimping found their way into surgical reports. Explanation of these and other physical properties of the various fabrics used to date have been well documented by numerous authors. (86, 115, 122, 332) The fabrics most commonly used experimentally and clinically and most thoroughly evaluated in the past 5 years have been vinyon N, nylon, orlon, teflon, and dacron.

Vinyon N: Aside from Voorhees and Blakemore, tubes of this material were used experimentally by D'Angelo, Benson, and Grimson (93) who found it quite satisfactory to bridge aortic defects in dogs but did find thrombotic occlusion in 8 of 20 animals. Deterling and Bhonsley, (122) after comparing its use with nylon, orlon, dacron, teflon, and

saran, stated a preference for dacron, orlon, and nylon, in that order. Deterling, (115) as did Edwards, (332) also felt that the contracting and stiffening which occurred upon subjection to autoclaving, preventing its being sterilized by this method, and the limited commercial output of the yarn, were definite disadvantages. Griffith and associates (180) used vinyon tubes in growing pigs with and without an interposed strip of autogenous artery. In the former group, they found 10 of 12 grafts satisfactory after 7 months, and in the latter all of the 18 observed were patent. Although there was some concern that this fabric might be carcinogenic because vinyl chloride has been found to be so in some strains of rodents, this has never been substantiated. In fact, in none of the plastics under discussion has this been observed. In a report by a Committee of the Society for Vascular Surgery (86) summarizing the status of cloth prostheses up to June, 1956, it was reported that in the aorta vinyon was successful in 86 per cent of 170 such animal grafts and 92 per cent of 49 clinically inserted protheses. In peripheral arteries the success rate was lower, being 39 per cent and 67 per cent for the experimental and clinical groups, respectively. Shortly thereafter, Shumacker and associates (432) reported that the poorest results obtained in their comparative study of various cloths were with vinyon N. No subsequent reports of the use of this material have come to our attention. It has been relegated to historical importance only.

Nylon: Early reports concerning the use of this material were those of Shumacker and associates (200, 431, 433) who used nylon grafts fused with polyethylene, either interposed or coated on the outside to eliminate porosity, and Self and colleagues (424) who inserted braided nylon dipped in liquid vinyl plastic. Although the incidence of thrombosis in both groups was significant, it was not as great as when smooth lined tubes, such as polyethylene, were used alone. (478) Apparently, as Edwards (137) pointed out, the thrombotic lining is more capable of attaching itself to the nylon fibers present in the lumen. Shumacker, (432) shortly after, advocated an uncoated nylon filter cloth.

A host of investigators almost simultaneously began to report their experiences with this fabric alone as a vessel replacement. Deterling (120, 122) documented some of its physical properties and reported excellent results in animal experiments. In a subsequent report about a year later he maintained his enthusiasm for its use.

Edwards and Tapp (139) introduced braided nylon tubes treated with silicone. They were made flexible by a permanent circular crimp to

avoid kinking—an important step forward toward the development of an ideal prosthesis. Moreover, the grafts were seamless, were machine made, and were the result of collaboration with the textile industry without which any future progress in this field will be impossible. An interesting monograph of the development and experience with these grafts has been compiled by Edwards. (137) In 1956, these authors (140) reported their results using crimped tube arterial grafts in extremities. Short term follow-up studies were excellent and led them to recommend abandonment of straight uncrimped cloth grafts in peripheral vessel replacement because of poor results. By 1957, (141) bifurcation grafts of crimped nylon were available.

Others to use nylon were Hufnagel (227, 228); Poth (385); Szilagyi (453) who preferred teflon; Ouzounian (373) who used yard goods nylon in dogs with excellent results; Whittlesey and associates (482) and Szilagyi and colleagues (455) who concerned themselves with the evaluation of elastic ("Helenca") nylon seamless sleeves and felt that they offered the greatest potential of all the synthetic grafts; Hardin (197) who used nylon grafts in 13 cases of symptomatic abdominal aneurysms in humans with good results; and Shumacker and associates (432) who felt that grafts of small diameter, either of nylon filter fabric or of braided nylon, were excellent as canine aortic prostheses—perhaps even better than homografts—and when used in 78 patients they proved excellent. (429) Others, (80, 201, 275) likewise, reported their findings.

The 1956 summary of the use of all types of nylon grafts as compiled by the Committee of the Society of Vascular Surgery (86) indicated that of 52 aortic prostheses inserted clinically, 94 per cent were successful, and of 72 such grafts used in peripheral arteries 79 per cent were considered a success. Whether or not these figures represented a true picture of the results in this country at that time is, of course, questionable. Recently, DeBakey, Crawford, Cooley, and Morris (103) published the results of their vast experiences and they recorded 95 per cent successful graft replacement in aorto-iliac occlusive disease using the "Edwards-Tapp" nylon crimped graft, and 86 per cent excellent results with this graft in treatment of femoro-popliteal occlusions.

It has been reported (204, 343) that nylon, because it has the highest moisture regain of any of the synthetics, tends to lose significant tensile strength. The greatest loss of strength occurs during the first 6 months with no further loss during the next year. (204) Of further interest

was the observation (246) that such grafts (and orlon) are capable of undergoing atheromatous degeneration just as homografts.

Orlon: Many of the same investigators (86, 103, 122, 197, 210, 228) who evaluated vinyon and nylon reported their experiences with orlon. It was felt that because of its low surface electrostatic change, a lowered incidence of thrombosis might be expected from its use. However, because of its ability to burn, its decreased ability to recover from stretch, its significant loss of tensile strength, and its high moisture regain, it would seem to have no apparent advantage over nylon. Wesolowski and Sauvage (478) reported a high incidence of "wrinkle-thrombosis" when it was used as a bifurcation prosthesis. In a summary of its use for grafting up to 1956 by the Committee previously mentioned, in the evaluation of the other materials (86) it was found that successful results were achieved in 96 per cent of 99 clinical cases where insertion was into the aorta, but in 19 patients on whom the grafts were used in the peripheral arterial system only 32 per cent were successful. Orlon is today no longer used as graft material.

Teflon: This synthetic material has offered promise because of its production of little tissue reaction, its being non-wetable, and its ability to maintain its strength over a long period of time. An increasing number of reports concerning its use as vascular grafts are now available. (86, 122, 138, 171, 332, 386, 453) Szilagyi and associates (453) found that seamless tubes of bleached teflon were far superior to other fabrics when used experimentally, as did Girvin's group (171) who used it in growing pigs. Encouraged by their success, they used teflon grafts clinically and were the first to report their clinical experience in 11 cases with this material manufactured as seamless tubes. (332) They felt, as did Pratt, (386) that this material better met their needs for a vascular substitute than did any other. Recently, Harrison, (202, 203) in an excellent experimental study in which he compared grafts of nylon, dacron, orlon, ivalon sponge, and teflon, found that the best and only satisfactory results were obtained with woven, purified teflon tubes. However, none of the synthetic prostheses was satisfactory for replacing blood vessels less than 5 mm. in diameter. The Edwards' type of crimped graft made of knitted teflon is now available commercially, and is the graft of choice by him. (138)

Dacron: The popularity of this material for grafts is presently increasing. Its ability to maintain its strength, its minimal water absorption and production of tissue reaction suggested its superiority. (86, 122) Elasticized dacron arterial prostheses have been evaluated by

Dale and Niguidula (89) and Szilagyi and associates. (448) The former compared fluflon dacron in canine peripheral vessels to other synthetic grafts, found it the easiest to handle, and suggested its clinical use but second to autogenous veins. The latter investigators found an excellent rate of patency, even when traversing a tortuous course, and low tissue reactivity. Their early results in patients were slightly inferior to that with homografts, but they were of the opinion that the late patency rate of such prostheses would be better than homografts. Knox and West (266) prepared their own dacron cloth grafts and reported their use in the management of 7 patients with obstruction of the superficial femoral artery. Success was achieved in only two.

DeBakey and associates (80, 103) have developed a crimped knitted tube and bifurcation prosthesis of dacron in cooperation with the Philadelphia Textile Institute. Its use as a graft replacement in 100 patients with aorto-iliac occlusive disease was 99 per cent successful. In 137 replacements of femoro-popliteal occlusions, it was 89 per cent effective. The number of late failures awaits a more prolonged period of observation. Our own experience with this prosthesis, although limited, had led us to feel that it is the easiest of all to handle and to technically insert. The fact that it needs no cuffing or heat sealing is advantageous, and the knowledge that the graft may be opened and re-sutured or have a side branch anastomosed to it is comforting. This type of prosthesis is readily available commercially.

Julian, Deterling, and associates (250, 251) in a combined effort from the University of Illinois and Columbia University have developed and evaluated woven dacron prostheses. It became readily apparent to them that the flat tubes were not at all satisfactory. They were thus subjected to crimping. Using this type of tube, 75 by-passes were performed. Sixty-eight were patent for at least 9 months. Twelve such woven bifurcation grafts have been inserted with success in all. This graft, both straight tube and bifurcation, is also marketed commercially.

It would seem that at present the use of manufactured dacron or teflon grafts are preferable to any of the other synthetic materials. With the entrance of surgical supply manufacturers into this field, it is conceivable that improved prostheses will constantly make their appearance. But to expect that after a point better grafts will mean better results is perhaps naive. With better grafts one must have concomitantly better case selection, better control of the progression of the patient's disease, and better technical proficiency. The grafts will never be so good that

they can be inserted with universal success by the surgeon untrained in the pitfalls of this field of surgery.

The question previously asked, "should homografts be abandoned?" might now be considered.

It would certainly seem that the popularity of arterial homografts is at a low ebb. This has occurred rather precipitously and is best demonstrated by the fact that in January, 1957 DeBakey (101) wrote: "At this time we believe that when available the homograft is the preferable replacement in view of its established durability and its versatility of application." By June, 1958, however, Cooley, (66) a colleague of DeBakey's, in discussing the merits of a particular dacron synthetic graft, said: ". . . I doubt whether any experimental evidence at this time would influence us to change back to homografts."

There seems to be little disagreement that for aortic-iliac replacement the newer "factory-made" prostheses of teflon or dacron are preferable to the homograft. Schenk, Cosgriff, and Gray, (417) however, in one of the very few physiologic studies made on vascular grafts, found that cloth prostheses implanted in the thoracic aorta markedly interfered with pulse wave transmission in contrast to the findings with homografts. They concluded that since a pulsatile flow is superior to a non-pulsatile one, arterial homografts have functional superiority, at least up to one year, over available prosthetic material. Clinically, we do not believe this has been substantiated. Such observations are further indicated. In vessels of the extremities, the synthetics have been less than ideal. In the experience of many, they have even been poorer than the homograft. In fact, they appear low on most lists of preference. We must wait a few years more for proper evaluation of these grafts. As far as we are concerned, little worthwhile information can be expected to result from those grafts inserted at the time when the material for them was purchased in a dry goods store and they were fashioned by hand in a variety of ways. With commercially available grafts, enough uniformity for future comparison and evaluation of data will exist.

We cannot help but believe that within a few years homografts of blood vessels will be relegated to historical significance.

VII.

While to many it has been an appealing concept to resect an obliterated blood vessel and restore its continuity by some form of prosthesis, and to others it has been more reasonable to by-pass the obstruction, a third group has advocated the restoration of blood flow in appropriate

circumstances by removal of the arterial thrombus through an arteriotomy. It is of interest that this latter group has had its greatest strength in France and in California in this country. In fact, the early history of the techniques for "disobliteration" of arterial thrombosis was first reviewed by Delbet (110, 277) in 1906 and 1911. At that time (1911) he wrote: "The easiest operation that can be done to cure arterial obstruction is incision of the artery, extraction of the thrombus and closure of the vessel." But he did add that in thrombosis due to endarteritis the clot re-forms, following removal, with great rapidity. These early attempts of treatment by this method were practically forgotten until dos Santos (127) in 1947 reported his experiences with endarterectomy. Within the next few years, several groups of French surgeons (11, 158, 285, 389, 390) reported their results, and, in general, favored this procedure. By 1950, Reboul and Laubry (390) were able to report their experiences from 93 such operations. They administered heparin for several days postoperatively to prevent recurrent thrombosis.

In this country, Wylie and colleagues (489) in 1951 reported the results of an experimental study whereby fascia lata was used to wrap vessels that were endarterectomized. Thromboendarterectomy was performed in 6 patients. These workers continued to accumulate experience with this technique, reporting their results in 1952, (486) 1953, (490) and 1955. (488) By 1955, 62 patients had been subjected to this operation—46 having aortic-iliac occlusion and 16 femoral occlusive disease. Normal or improved circulation was established in 47. That Wylie (487) has not wavered in his preference of treatment after 8 years of experience with thromboendarterectomy is apparent when he recently (1959) said: "We have held that thromboendarterectomy is the most suitable method of treatment for all operable arteriosclerotic lesions, regardless of their extent or location." At about the same time, Barker and Cannon (8, 9, 46) were reporting their experiences and finding that with proper case selection 95 per cent will have excellent results. Long term follow-up (9) failed to reveal late thrombotic or atheromatous obstruction of an adequately endarterectomized segment of artery. Others (163, 205, 325, 402, 481) have reported success by this procedure in a small number of cases, while Coelho, Leeds, and Freeman (61) followed 19 patients one to 39 months thromboendarterectomized for occlusion of the terminal aorta or common iliac arteries. All but one had excellent results. Intra-arterial heparinization was carried out postoperatively from one to 8 days. Recently (1959) Freeman and Nicholson (164) reported on 87 thromboendarterectomies.

In those patients operated upon for claudication, 76 per cent of the cases followed 6 months to 6 years received relief; 70 per cent of those operated for ischemia had healing of their lesions or were relieved of pain. Linton (293, 295) has indicated that his choice of treatment for femoral artery obstruction is (1) venous autograft, and (2) thromboendarterectomy. Muller, Liddle, and Edmunds, (348) having followed 32 endarterectomized patients for more than 6 months, felt that the over-all results following thromboendarterectomy are superior to by-pass grafting, especially where smaller vessels are concerned. Bergan (18) of Oslo, Norway, has indicated that this procedure and anticoagulants are his preference for treatment of obliterative arteriosclerosis. A lack of enthusiasm for this procedure exists in the report of Warren (472) who considers it as an alternative method to reconstruction by the by-pass technique.

Perhaps the reason why thromboendarterectomy in this country has been slow in evaluation and popularity may be because of the outstanding results obtained with grafting procedures by DeBakey and associates, (103) who could not help but set standards and influence trends of vascular surgery in this country through their magnificent publications. They, too, however, have performed endarterectomy for aorto-iliac occlusions and reported success. In femoral popliteal occlusions their results with endarterectomy were inferior to other procedures.

Our own experience with endarterectomy has been most gratifying and is the procedure of choice when feasible. Segments of vessel as extensive as the entire superficial femoral or the external iliac common femoral arteries have been handled in this fashion with excellent results. We have not hesitated to use heparin postoperatively in those individuals on whom an extensive disobliteration of the leg vessels was performed. And, in fact, many of these patients, particularly where the popliteal artery has been involved, have been discharged from the hospital to receive dicoumerol (Coumadin) indefinitely. For aortic or iliac thromboendarterectomy we do not use anticoagulants. In almost all cases we transect the vessel at the most distal point of endarterectomy and then re-anastomose it. In this fashion the intimal "flap" that remains is eliminated. At this time, endarterectomy is our procedure of first choice for the treatment of segmental obliterative disease.

The recent application of Longmire, Cannon, and Kattus (47, 299) of the technique of endarterectomy to the coronary vessels of patients with angina pectoris and to atherosclerotic occlusion of the internal carotid artery (167, 188) suggests that possibly there is potential use-

fulness for the procedure in smaller vessels where grafting is not feasible. Further evaluation is necessary.

VIII.

Clinical vascular surgery seems to have just about passed through that gregarious period of claims and counter-claims, inflated optimism, and pessimism which so often characterizes new therapeutic endeavors. Within the past decade, the basic principles of such surgery, as originally established in the laboratory by Guthrie and his contemporaries at the turn of the century, were gathered up, embellished, tested, sorted, and evaluated. It seemed that now was a proper time for a "summing-up" of what has happened.This is the purpose of the preceding review.

While homografts have not stood up to the test of time and their popularity has distinctly waned, they certainly have served a useful purpose. They functioned well long enough to demonstrate the great success that might be expected from the vascular surgery of trauma, congenital defects, aneurysm, and segmental thrombotic disease. That their replacements—synthetic prostheses—represent the ideal, is not so. The ultimate fate of the commercially manufactured teflon and dacron grafts now being used must await the passage of more years. They are, however, foreign material implanted into the human body and, as such, may be expected to instigate a host response of greater or lesser magnitude. It is to be hoped that further effort will result in the production of consistently less irritating materials evoking foreign body reactions which in no way interfere with the prolonged functional integrity of the graft. Progress toward this end will now be slower, but the likelihood of attaining such a goal is not beyond the realm of possibility.

It has been suggested that should the immunologic barrier to homotransplants be overcome, vascular homografts might once again have the position of prominence. This is unlikely. For, in our opinion, the degenerative changes now observed following the use of preserved homografts are not the result of the classical immunologic host-graft response and, therefore, alteration of this mechanism will contribute only insofar as the use of fresh homologous blood vessels are concerned. It has already been demonstrated that the logistics involved preclude their use.

Our feeling is that thromboendarterectomy, particularly in smaller blood vessels, with the judicious use of anticoagulants has not yet reached its crest of popularity. Undoubtedly better techniques will be devised for the accomplishment of this procedure. At present, we

feel that the perfectly performed, initially successful thromboendarterectomy is preferable to the initially successful synthetically implanted graft.

The future reputation that vascular surgery attains and the success rate achieved, as in all of surgery, will depend upon judicious case selection and the utilization of therapeutic procedures which are most applicable and most successful in the hands of the individual surgeon. Just as in surgery for cancer or for inflammation, if "lines of resection" are not free of disease, there is little reason to be optimistic about long-term therapeutic triumphs. To expect prolonged success when the distal end of a by-pass graft is anastomosed to a vessel with intimal disease or one harboring further thrombosis beyond is unreasonable.

We fully expect that vascular surgery will be applied to smaller and smaller vessels, for such is possible and will be utilized by those who are willing to master the technical skill. In our laboratory, end-to-side portacaval shunt is being performed by Dr. S. H. Lee on 300 gm. rats with routine success by the same suture technique used in humans (7-0 silk), and the vascular anastomoses remain patent indefinitely. Such technical gymnastics might well be clinically utilizable. Particularly would this be so if organ transplantation became feasible. Of course, the smaller the blood vessel operated upon, the narrower becomes the permissible technical error that is compatible with success.

Obviously, surgery for arteriosclerotic occlusive disease, just as with surgery for neoplasm, is a delaying action until such time as a more rationale approach can be undertaken, i.e., prevention of the process. Until that time, however, countless people have been and will be given the opportunity to walk on their own extremities, rather than on artificial ones, with freedom from the miserable sequellae attendant with ischemia. Many others continue to live because their vascular aneurysms have been eliminated.

To Claude Guthrie and his contemporaries we owe a debt of gratitude. They provided us with a heritage, w[illegible] though we were slow to appreciate, set the stage for the pres[illegible] ishments in the f[illegible] vascular surgery. But, we, too, [illegible] legacy. So surgeons and their colleagues in oth[illegible] realize that th[illegible] mental surgical laboratory and the [illegible] arable, we [illegible] no fear concerning that score.

BIBLIOGRAPHY AND REFERENCES

1. Abraham A., and Sin, L. Microscopic Innervation of Fixed Vascular Grafts. *Acta. Morph. Hung.* 5:103-112,1955.
2. Androsov, P. I. New Method of Surgical Treatment of Blood Vessel Lesions. *A.M.A. Arch. Surg.* 73:902-910, 1956.
3. Ayers, W. B., Cincotti, J. J., and Gliedman, M. L. Experiences with Ivalon (Polyvinyl Formalinized) Sponge Prostheses for Vascular Replacements. *A.M.A. Arch. Surg.* 74:173-182, 1957.
4. Bacigalupo, F., Simandl, E., Bhonslay, S. B., and Deterling, R. A., Jr. The Effect of Heparinization Upon Vascular Healing. *A.M.A. Arch. Surg.* 74:153-172, 1957.
5. Bahnson, H. T. Considerations in Excision of Aortic Aneurysms. *Ann. Surg.* 138:377-386, 1953.
6. ———. Treatment of Abdominal Aortic Aneurysm by Excision and Replacement by Homograft. *Circulation*, N. Y. 9:494-503, 1954.
7. ———. Surgical Treatment of Aortic Aneurysm and Aortic Thrombosis. *Postgrad. M.* 19:7-15, 1956.
8. Barker, W. F., and Cannon, J. A. An Evaluation of Endarterectomy. *A.M.A. Arch. Surg.* 66:488-495, 1953.
9. ———. Late Results Following Endarterectomy. *West. J. Surg.* 63:562-566, 1955.
10. Batzner, K., and Grupp, G. Über die Konservierung von Artérientransplantaten, den Einfluss von Artérientransplantation, den Einflusse von Kaelte and Sauerstoffmangel, und Eine Methode zur Schnellen Feststelling Ihrer Lebensfaehigkeit. *Dtsch. Zschr. Chir.* 299:122, 1951.
11. Bazy, L., Hucuier, J., Reboul, H., and Laubry, P. Technique des "Endartériectomies" pour Artérites Obliterantes Chroniques des Membres Inférieurs, des Iliaques et de l'Aorte Abdominale Inférieure. *J. chir.*, Par. 65:196-210, 1949.
12. Beck, C. S. Revascularization of the Heart. *Ann. Surg.* 128:854-864, 1948.
13. Beck, C. S., McKhann, C. F., and Belnap, W. D. Revascularization of the Brain Through the Establishment of a Cervical Arteriovenous Fistula. *J. Pediat.*, S. Louis 35:317-329, 1949.
14. Beck, C. S., Stanton, E., Batiuchok, W., and Leiter, E. Revascularization of Heart by Graft of Systemic Artery into the Coronary Sinus. *J. Am. M. Ass.* 137:436-442, 1948.
15. Bencini, A., and Bellinazzo, P. Contributo Sperimentale Allo Studio dei Trapianti Arteriosi Omoplastici: le vie di Nutrizione e di Sosteituzione Tissurale. *Arch. ital. chir.*, Bologna 76:439-467, 1953.
16. ———. Experimental Studies of the Fate of Arterial Homografts. *Angiology* 4:483-495, 1953.
17. Benjamin, R. B., Turbak, C. E., Hannon, D. W., Shumway, N. E., and Lewis, F. J. Polyvinyl Sponge in Experimental Surgery. *Ann. Surg.* 145:509-516, 1957.

18. Bergan, F. Thrombendarterectomy for Obliterative Arteriosclerosis. *J. Am. M. Ass.* 168:923, 1958 (Norway-Foreign Letters).
19. Berman, J. K., Boyd, F. J., Jr., and Saint, W. K. The Treatment of Thoracic and Abdominal Aneurysms of Syphilitic and Arteriosclerotic Origins: Preliminary Report. *J. Indiana M. Ass.* 42:889-893, 1949.
20. Bernheim, B. M. Arteriovenous Anastomosis: Reversal of the Circulation—as a Preventive of Gangrene of the Extremities: Review of the Literature and Report of Six Additional Cases. *Ann. Surg.* 55:195-207, 1912.
21. ———. The Ideal Operation for Aneurisms of the Extremity: Report of a Case. *Bull. Johns Hopk. Hosp.* 27:93-95, 1916.
22. ———. Blood-Vessel Surgery in the War. *Surg. Gyn. Obst.* 30:564-567, 1920.
23. ———. Arteriovenous Anastomosis: Follow-up After Eighteen Years of "Successful Reversal of the Circulation in all Four Extremities of the Same Individual." *J. Am. M. Ass.* 96:1296-1297, 1931.
24. ———. Management of Vascular Injuries. *Surg. Clin. N. America* 22:1417-1426, 1942.
25. Bickham, W. S. Arteriovenous Aneurysms. *Ann. Surg.* 39:767-775, 1904.
26. Blades, B. B. Discussion of Paper by E. J. Poth, J. K. Johnson and J. H. Childers, "The Use of Plastic Fabrics as Arterial Prostheses." *Ann. Surg.* 142:624-632, 1955.
27. Blakemore, A. H. The Clinical Behavior of Arteriosclerotic Aneurysm of the Abdominal Aorta: A Rational Surgical Therapy. *Ann. Surg.* 126:195-207, 1947.
28. Blakemore, A. H., and Fitzpatrick, H. F. The Surgical Management of the Post-splenectomy Bleeder with Extra-Hepatic Portal Hypertension. *Ann. Surg.* 134:420-432, 1951.
29. Blakemore, A. H., and King, B. G. Electrothermic Coagulation of Aortic Aneurysms. *J. Am. M. Ass.* 111:1821-1827, 1938.
30. Blakemore, A. H., and Lord, J. W., Jr. A Non-Suture Method of Blood Vessel Anastomosis; Experimental and Clinical Study. *J. Am. M. Ass.* 127:685, 1945.
31. ———. The Technique of Using Vitallium Tubes in Establishing Portacaval Shunts for Portal Hypertension. *Ann. Surg.* 122:476-489, 1945.
32. Blakemore, A. H., Lord, J. W., Jr., and Stefko, P. L. The Severed Primary Artery in the War Wounded: A Nonsuture Method of Bridging Arterial Defects. *Surgery* 12:488-508, 1942.
33. Blakemore, A. H., and Voorhees, A. B., Jr. The Use of Tubes Constructed from Vinyon "N" Cloth in Bridging Arterial Defects: Experimental and Clinical. *Ann. Surg.* 140:324-334, 1954.
34. Blalock, A., and Taussig, H. B. The Surgical Treatment of Malformations of the Heart in Which There is Pulmonary Stenosis or Pulmonary Atresia. *J. Am. M. Ass.* 128:189-202, 1945.
35. Blum, L., Medl, W. T., and Keefer, E. B. C. Aortic Homograft Substitution for the Post Renal Inferior Vena Cava. *A.M.A. Arch. Surg.* 72:567-570, 1956.
36. Bode, E., and Fabian, E. Uber die Transplantation Freier und Konservierter Gefäese. *Beitr. klin. Chir.* 66:67-84, 1910.
37. Brock, R. C. Aortic Homografting. A Report of Six Successful Cases. *Guy's Hosp. Rep.*, Lond. 102:204-228, 1953.
38. Brooks, B. Intra-Arterial Injection of Sodium Iodid: Preliminary Report. *J. Am. M. Ass.* 82:1016-1019, 1924.
39. ———. Surgical Application of Therapeutic Venous Obstruction. *A.M.A. Arch. Surg.* 19:1-23, 1929.

40. Brooks, B., Johnson, G. S., and Kirtley, J. A., Jr. I. Simultaneous Vein Ligation; An Experimental Study of the Effect of Ligation of the Concomitant Vein on the Incidence of Gangrene Following Arterial Obstruction. *Surg. Gyn. Obst.* 59:496-500, 1934.
41. Brooks, B., and Martin, K. A. Simultaneous Ligation of Vein and Artery: An Experimental Study. *J. Am. M. Ass.* 80:1678-1681, 1923.
42. Brunnen, R. L. The Preparation and Preservation of Arterial Homografts: Experimental Study. *Guy's Hosp. Rep.*, Lond. 102:194-203, 1953.
43. Bryant, M. F., Jr., Lazenby, W. D., and Howard, J. M. Experimental Replacement of Short Segments of Veins. *A.M.A. Arch. Surg.* 76: 289-293, 1958.
44. Callander, C. L. Study of Arteriovenous Fistula with Analysis of 447 Cases. *Ann. Surg.* 71:428-459, 1920.
45. Campbell, H. A., and Link, K. P. Studies on the Hemorrhagic Sweet Clover Disease. IV. The Isolation and Crystallization of the Hemorrhagic Agent. *J. Biol. Chem.* 38:21-33, 1941.
46. Cannon, J. A., and Barker, W. F. Successful Management of Obstructive Femoral Arteriosclerosis by Endarterectomy. *Surgery* 38:48-60, 1955.
47. Cannon, J. A., and Longmire, W. P., Jr. Considerations of the Rationale and Technique of Coronary Endarterectomy for Angina Pectoris. Presented at Meeting of Society of University Surgeons, Denver, Colo., Feb. 14, 1959.
48. Carrel, A. Results of the Transplantation of Blood Vessels, Organs and Limbs. *J. Am. M. Ass.* 51:1662-1667, 1908.
49. ———. Latent Life of Arteries. *J. Exp. M.* 12:460-486, 1910.
50. ———. Permanent Intubation of the Thoracic Aorta. *J. Exp. M.* 16:17-24, 1912.
51. ———. Results of the Permanent Intubation of the Thoracic Aorta. *Surg. Gyn. Obst.* 15:245-248, 1912.
52. ———. The Preservation of Tissues and its Applications in Surgery. *J. Am. M. Ass.* 59:523-527, 1912.
53. Carrel, A., and Guthrie, C. C. Uniterminal and Biterminal Venous Transplantations. *Surg. Gyn. Obst.* 2:266-286, 1906.
54. Castellanos, A., and Pereiras, R. Counter-Current Aortography. *Rev. cubana de cardiol.* 2:187-205, 1940.
55. Castellanos, A., Pereiras, R., and Garcia, A. La Angio-cardiografia Radio-opaca. *Arch. estud. clin.* Habana, 1937.
56. Charles, A. F., and Scott, D. A. Studies on Heparin: (1) The preparation of Heparin. *J. Biol. Chem.* 102:425-429, 1933.
57. ———. Studies on Heparin: (2) Heparin in Various Tissues. *J. Biol. Chem.* 102:431-435, 1933.
58. ———. Studies on Heparin: (3) The Purification of Heparin. *J. Biol. Chem.* 102:437-448, 1933.
59. Cockett, F. B. Personal communication to: Linton, R. R. and Menendez, C. V. *Ann. Surg.* 142:568-585, 1955.
60. Cockett, F. B., and Norman, A. G. Late Results of Direct Surgery of the Aortic Bifurcation and Its Major Branches. *Brit. M. J.* 1:727-734, 1958.
61. Coelho, H. M., Leeds, F. H., and Freeman, N. E. Arteriosclerotic Occlusion of the Terminal Aorta and Common Iliac Arteries Treated by Thromboendarterectomy. *Surgery* 37:105-114, 1955.
62. Coleman, C. C., Jr., Deterling, R. A., Jr., and Parshley, M. S. Experimental Studies of Preserved Aortic Homografts. *Ann. Surg.* 134:868-877, 1951.

63. ———. Some Long-term Observations on Aortic Homografts. *Surgery* 37:64-79, 1955.

64. CONN, J. H., and SPARKUHL, K. Arterial Homografts: Experience with End-to-Side Vascular Anastomosis. *Am. J. Surg.* 94:695-704, 1957.

65. COOKE, F. N., HUGHES, C. W., JAHNKE, E. J., and SEELEY, S. F. Homologous Arterial Grafts and Autogenous Vein Grafts Used to Bridge Large Arterial Defects in Man. *Surgery* 33:183-189, 1953.

66. COOLEY, D. A. Discussion of paper by Dale, W. A. and Niguidula, F. N., "Study of Elasticized Dacron as Arterial Prosthesis." *A.M.A. Arch. Surg.* 78:246-259, 1959.

67. COOLEY, D. A., and DEBAKEY, M. E. Surgical Considerations of Intrathoracic Aneurysms of the Aorta and Great Vessels. *Ann. Surg.* 135:660-680, 1952.

68. ———. Surgical Considerations of Excisional Therapy for Aortic Aneurysms. *Surgery* 34:1005-1020, 1953.

69. ———. Resection of the Thoracic Aorta with Replacement by Homograft for Aneurysms and Constrictive Lesions. *J. Thorac. Surg.* 29:66-104, 1955.

70. ———. Resection of Entire Ascending Aorta in Fusiform Aneurysm using Cardiac By-pass. *J. Am. M. Ass.* 162:1158-1159, 1956.

71. COOLEY, D. A., DEBAKEY, M. E., and CREECH, O., JR. Surgical Treatment of Aortic Aneurysms. *Am. Surgeon* 22:1043-1051, 1956.

72. COOLEY, D. A., DEBAKEY, M. E., and MORRIS, G. C., JR. Controlled Extracorporeal Circulation in Surgical Treatment of Aortic Aneurysm. *Ann. Surg.* 146:473-486, 1957.

73. COOLEY, D. A., MAHAFFEY, D. E., and DEBAKEY, M. E. Total Excision of the Aortic Arch for Aneurysm. *Surg. Gyn. Obst.* 101:667-672, 1955.

74. CORRADI. Cited by Dean D. Lewis in *Practice of Surgery.* J. B. Lippincott Co., Vol. 12, Chapter 5 E, 1879.

75. COWELL, E. M. Simultaneous Ligature of Arterial and Venous Trunks in War Surgery. *Brit. M. J.* 1:577-578, 1917.

76. CRAFOORD, C., and NYLIN, G. Congenital Coarctation of Aorta and Its Surgical Treatment. *J. Thorac. Surg.* 14:347-361, 1945.

77. CRAWFORD, E. S., CREECH, O., JR., COOLEY, D. A., and DEBAKEY, M. E. Treatment of Arteriosclerotic Occlusive Disease of the Lower Extremities by Excision and Graft Replacement or By-pass. *Surgery* 38:981-992, 1955.

78. ———. Treatment of Arteriosclerotic Occlusive Disease in 101 Lower Extremities by Arterial Homografts. *South M. J.* 49:665-670, 1956.

79. CRAWFORD, E. S., and DEBAKEY, M. E. The By-pass Operation in the Treatment of Arteriosclerotic Occlusive Disease of the Lower Extremities. *Surg. Gyn. Obst.* 101:529-535, 1955.

80. CRAWFORD, E. S., DEBAKEY, M. E., and COOLEY, D. A. Clinical Use of Synthetic Arterial Substitutes in Three Hundred Seventeen Patients. *A.M.A. Arch. Surg.* 76:261-270, 1958.

81. CREECH, O., JR. Personal communication to Edwards, W. S., "Plastic Arterial Grafts." C. T. Thomas, 1957, Springfield, Ill., pp. 126.

82. CREECH, O., JR., DEBAKEY, M. E., COOLEY, D. A., and HALPERT, B. Structural Alterations in Human Aortic Homografts One to Two and One-Half Years After Transplantation. *Surg. Gyn. Obst.* 103:147-154, 1956.

83. CREECH, O., JR., DEBAKEY, M. E., COOLEY, D. A., and SELF, M. M. Preparation and Use of Freeze-dried Arterial Homografts. *Ann. Surg.* 140:35-43, 1954.

84. CREECH, O., JR., DEBAKEY, M. E., and MAHAFFEY, D. E. Total Resection of the Aortic Arch. *Surgery* 40:817-830, 1956.

85. CREECH, O., JR., DEBAKEY, M. E., SELF, M. M., and HALPERT, B. The Fate of Heterologous Arterial Grafts: An Experimental Study. *Surgery* 36:431-444, 1954.

✓86. CREECH, O., JR., DETERLING, R. A., JR., EDWARDS, S., JULIAN, O. C., LINTON, R. R., and SHUMACKER, H., JR. Vascular Prostheses—Report of the Committee for the Study of Vascular Prostheses of the Society of Vascular Surgery. *Surgery* 41:62-80, 1957.

87. CREECH, O., JR., JORDAN, G. L., JR., DEBAKEY, M. E., OVERTON, R. C., and HALPERT, B. The Effect of Chronic Hypercholesterolemia on Canine Aortic Transplants. *Surg. Gyn. Obst.* 101:607-614, 1955.

88. CULLEN, M. L., STEPPACHER, L. G., GREENSPAN, B., MILLIKEN, H. E., JR., MOORE, G. W., and MORRIS, G. C., JR. Studies on the Effects of Concomitant Venous Ligation in Acute Arterial Occlusion. *Surg. Gyn. Obst.* 89:722-726, 1949.

89. DALE, W. A., and NICUIDULA, F. N. Study of Elasticized Dacron as Arterial Prosthesis. *A.M.A. Arch. Surg.* 78:246-259, 1959.

90. DALE, W. A., DEWEESE, J. A., and SCOTT, W. J. M. Autogenous Venous Shunt Grafts. Presented to Society of University Surgeons Meeting, Denver, Colo., Feb. 13, 1959.

91. DALEM, J. LaGreffe du Carrefour Aortique Chez le Chien. *Acta chir. belg.* 49:759-777, 1950.

92. D'ALLAINES, F., and OECONOMOS, N. Les Greffes Vasculaires: Etude Expérimentale Précédant la Création d'une Banque d'artéres. *Mem. Acad. chir., Par.* 76:707-723, 1950.

93. D'ANGELO, G. J., BENSON, W. R., and GRIMSON, K. S. Vinyon-N Cloth Tube for Bridging Arterial Defects. *A.M.A. Arch. Surg.* 70:39-44, 1955.

✓94. DANIEL, W. W. Bridging Defects in the Canine Portal and Superior Mesenteric Veins with Plastic Tubes and Vascular Grafts: A Preliminary Report. *Cancer* 5:1041-1048, 1952.

95. DAVIS, J. H., BENSON, J. W., and MILLER, R. C. Thoracoabdominal Aneurysm Involving Celiac, Superior Mesenteric and Renal Arteries. *A.M.A. Arch. Surg.* 75:871-876, 1957.

✓96. DEBAKEY, M. E. Cited by Deterling, R. A., and Bhonslay, S. V. "Use of Vessel Grafts and Plastic Prostheses for Relief of Superior Vena Caval Obstruction." *Surgery* 38:1008-1026, 1955.

97. ———. Dissecting Aneurysm of the Aorta: Editorial. *Surg. Gyn. Obst.* 102:372-373, 1956.

98. DEBAKEY, M. E., and COOLEY, D. A. Successful Resection of Aneurysm of Thoracic Aorta and Replacement by Graft. *J. Am. M. Ass.* 152:673-676, 1953.

99. ———. Surgical Treatment of Aneurysms of Abdominal Aorta by Resection and Restoration of Continuity with Homograft. *Surg. Gyn. Obst.* 97:257-266, 1953.

100. DEBAKEY, M. E., COOLEY, D. A., and CREECH, O., JR. Surgical Considerations of Dissecting Aneurysm of the Aorta. *Ann. Surg.* 142:586-612, 1955.

101. DEBAKEY, M. E., and CRAWFORD, E. S. Vascular Prostheses. *Transpl. Bull.* 4:2-4, 1957.

102. DEBAKEY, M. E., CRAWFORD, E. S., COOLEY, D. A., and MORRIS, G. C., JR. Successful Resection of Fusiform Aneurysm of Aortic Arch with Replacement by Homograft. *Surg. Gyn. Obst.* 105:657-664, 1957.

103. ———. Surgical Considerations of Occlusive Disease of the Abdominal Aorta and Iliac and Femoral Arteries: Analysis of 803 Cases. *Ann. Surg.* 148:306-324, 1958.

104. DEBAKEY, M. E., CRAWFORD, E. S., CREECH, O., JR., and COOLEY, D. A. Arterial Homografts for Peripheral Arteriosclerotic Occlusive Disease. *Circulation*, N. Y. 15:21-30, 1957.

105. DEBAKEY, M. E., CREECH, O., JR., and COOLEY, D. A. Occlusive Disease of the Aorta and Its Treatment by Resection and Homograft Replacement. *Ann. Surg.* 140:290-310, 1954.

106. DEBAKEY, M. E., CREECH, O., JR., COOLEY, D. A., and HALPERT, B. Structural Changes in Human Aortic Homografts. Study of Ten Cases. *A.M.A. Arch. Surg.* 69:472-482, 1954.

107. DEBAKEY, M. E., CREECH, O., JR., and MORRIS, G. C., JR. Aneurysm of Thoracoabdominal Aorta Involving the Celiac, Superior Mesenteric, and Renal Arteries: Report of 4 Cases Treated by Resection and Homograft Replacement. *Ann. Surg.* 144:549-573, 1956.

108. DEBAKEY, M. E., and SIMEONE, F. A. Battle Injuries of the Arteries in World War II. An Analysis of 2,471 Cases. *Ann. Surg.* 123:534-579, 1946.

109. DECAMP, P. T. Blood Vessel Grafting: Indications and Techniques. *Surg. Clin. N. America* 33:1039-1048, 1953.

110. DELBET, P. Chirurgie Artérielle et Veineuse. *Les Modernes Acquisitions.* Par., J-B. Baillière & fils, 1906, pp. 104.

111. DELORME, E. Surgical Treatment of Aneurysm of Aorta. *Bull. Acad. méd.*, Par. 85:582, 1921.

112. DENMAN, F. R., BROWN, W. G., SKINNER, S. J., FITCH, E. A., and GLASS, H. G. Fate of Human Aortic Homografts Ten, Twenty-four and Twenty-seven Months After Transplantation. *A.M.A. Arch. Surg.* 76:944-950, 1958.

113. DETAKATS, G., and MARSHALL, M. R. Surgical Treatment of Arteriosclerotic Aneurysms of the Abdominal Aorta. *A.M.A. Arch. Surg.* 64:307-319, 1952.

114. DETAKATS, G. Anticoagulant Therapy. *Surgery* 34:985-1001, 1953.

115. DETERLING, R. A., JR. Factors Influencing the Behavior of Synthetic Prostheses in the Vascular System. *Transpl. Bull.* 3:125-127, 1956.

116. ———. Discussion of paper by Lord, J. W., and Stone, P. W., "Use of Autologous Venous Grafts in the Peripheral Arterial System." *A.M.A. Arch. Surg.* 74:71-79, 1957.

117. ———. Cited by Weslowski, S. A., and Sauvage, L. R. "Heterologous Aortic Grafts—With Special Reference to Recipient Site, Ethylene Oxide Freeze-dry Preparation and Species of Origin." *Ann. Surg.* 145:187-193, 1957.

118. ———. Experience with Permanent By-pass Grafts in Treatment of Occlusive Arterial Disease. *A.M.A. Arch. Surg.* 76:247-260, 1958.

119. DETERLING, R. A., JR., and BHONSLAY, S. B. Use of Vessel Grafts and Plastic Prostheses for Relief of Superior Vena Caval Obstruction. *Surgery* 38:100[illegible]-1026, 1955.

120. ———. An Appraisal of Woven Synthetic Prostheses in the Vascular System *A.M.A. Arch. Surg.* 72:76-91, 1956.

121. DETERLING, R. A., JR., COLEMAN, C. C., JR., and PARSHLEY, M. S. Experimental Studies of the Frozen Homologous Aortic Graft. *Surgery* 29:419-[illegible], 1951.

122. DETERLING, R. A., JR., and BHONSLAY, S. B. An Evaluation of Synthetic Materials and Fabrics Suitable for Blood Vessel Replacement. *Surgery* 38:71-89, 1955.

123. Diaz Sarasola, R. Un caso de Operación de San Mártin. (Contribución a la Casuistica). *Arch. cardiol. y hemat.* 10:137-143, 1929.

124. Dickinson, P. H. The Suitability of Skin as a Strengthening Material for Vein Grafts: An Experimental Study. *Brit. J. Surg.* 44:529-537, 1957.

125. Donovan, T. J. The Use of Plastic Tubes in the Reparative Surgery of Battle Injuries to Arteries With and Without Intra-Arterial Heparin Administration. *Ann. Surg.* 130:1024-1043, 1949.

126. Doss, A. K., Thomac, H. C., and Bond, T. B. Renal Arteriography, its Clinical Value. *Texas J. Med.* 38:277-280, 1942.

127. dos Santos, J. C. Sur la Désobstruction des Thromboses Artérielles Anciennes. *Mem. Acad. chir.*, Par. 73:400-411, 1947.

128. dos Santos, R., Lamas, A., and Pereira, C. J. L'Arteriographie des Membres de L'Aorte et ses Brances Abdominales. *Bull. Soc. nat. chir.*, Par. 55:587-601, 1929.

129. dos Santos, R., Lamas, A., and Caldas, J. P. *Artériographie des Membres et de l'Aorte Abdominale: Préface du Leriche.* Masson & Cie, pp. 192, 1931.

130. Dubost, C., Allary, M., and Oeconomos, N. A Propos du Traitement des Anévrysmes de l'Aorte. Ablation de l'Anévrysme Rétablissment de la Continuité par Greffe d'Aorte Humaine Conservée. *Mem. Acad. chir.*, Par. 77:381-383, 1951.

131. ———. Resection of an Aneurysm of the Abdominal Aorta. *A.M.A. Arch. Surg.* 64:405-408, 1952.

132. Dye, W. S., Grove, W. J., Olwin, J. H., and Julian, O. C. Two- to Four-Year Behavior of Vein Grafts in Lower Extremities. *A.M.A. Arch. Surg.* 72:64-68, 1956.

133. Dye, W. S., Olwin, J. H., and Julian, O. C. Further Considerations on the Indications for and Limitations of Direct Surgery in Arteriosclerosis. *Circulation*, N.Y. 8:708-714, 1953.

134. Eastcott, H. H. G. Arterial Grafting for the Ischaemic Lower Limb. *Ann. R. Coll. Surgeons*, England 13:177-198, 1953.

135. Eastcott, H. H. G., Holt, L. B., Peacock, J. H., and Rob, C. G. Preservation of Arterial Grafts by Freeze-Drying: A Simplified Method. *Lancet*, Lond. 266:1311-1314, 1954.

136. Eastcott, H. H. G., and Hufnagel, C. A. The Preservation of Arterial Grafts by Freezing. *Surg. Forum* 1:269-282, 1950.

137. Edwards, W. S. *Plastic Arterial Grafts.* C. C. Thomas, Springfield, Ill., 1957, pp. 126.

138. ———. Progress in Synthetic Graft Development—An Improved Crimped Graft of Teflon. *Surgery* 45:298-309, 1959.

139. Edwards, W. S., and Tapp, J. S. Chemically Treated Nylon Tubes as Arterial Grafts. *Surgery* 38:61-70, 1955.

140. ———. Peripheral Artery Replacement and Chemically Treated Nylon Tubes. *Surg. Gyn. Obst.* 102:443-449, 1956.

141. ———. A Flexible Aortic Bifurcation Graft of Chemically Treated Nylon. *Surgery* 41:723-728, 1957.

142. Egdahl, R. H. Silicone Rubber as Grafting Material. *A.M.A. Arch. Surg.* 71:694-696, 1955.

143. Egdahl, R. H., and Hume, D. M. Nonsuture Blood-Vessel Anastomosis: An Experimental Study Using Polyethylene as Prosthetic Material. *A.M.A. Arch. Surg.* 72:232-240, 1956.

144. Egdahl, R. H., Hume, D. M., and Schlang, H. A. Plastic Venous Prostheses. *Surg. Forum* 5:235-241, 1954.

103. ———. Surgical Considerations of Occlusive Disease of the Abdominal Aorta and Iliac and Femoral Arteries: Analysis of 803 Cases. *Ann. Surg.* 148:306-324, 1958.

104. DEBAKEY, M. E., CRAWFORD, E. S., CREECH, O., JR., and COOLEY, D. A. Arterial Homografts for Peripheral Arteriosclerotic Occlusive Disease. *Circulation*, N. Y. 15:21-30, 1957.

105. DEBAKEY, M. E., CREECH, O., JR., and COOLEY, D. A. Occlusive Disease of the Aorta and Its Treatment by Resection and Homograft Replacement. *Ann. Surg.* 140:290-310, 1954.

106. DEBAKEY, M. E., CREECH, O., JR., COOLEY, D. A., and HALPERT, B. Structural Changes in Human Aortic Homografts. Study of Ten Cases. *A.M.A. Arch. Surg.* 69:472-482, 1954.

107. DEBAKEY, M. E., CREECH, O., JR., and MORRIS, G. C., JR. Aneurysm of Thoracoabdominal Aorta Involving the Celiac, Superior Mesenteric, and Renal Arteries: Report of 4 Cases Treated by Resection and Homograft Replacement. *Ann. Surg.* 144:549-573, 1956.

108. DEBAKEY, M. E., and SIMEONE, F. A. Battle Injuries of the Arteries in World War II. An Analysis of 2,471 Cases. *Ann. Surg.* 123:534-579, 1946.

109. DECAMP, P. T. Blood Vessel Grafting: Indications and Techniques. *Surg. Clin. N. America* 33:1039-1048, 1953.

110. DELBET, P. Chirurgie Artérielle et Veineuse. *Les Modernes Acquisitions.* Par., J-B. Baillière & fils, 1906, pp. 104.

111. DELORME, E. Surgical Treatment of Aneurysm of Aorta. *Bull. Acad. méd.*, Par. 85:582, 1921.

112. DENMAN, F. R., BROWN, W. G., SKINNER, S. J., FITCH, E. A., and GLASS, H. G. Fate of Human Aortic Homografts Ten, Twenty-four and Twenty-seven Months After Transplantation. *A.M.A. Arch. Surg.* 76:944-950, 1958.

113. DETAKATS, G., and MARSHALL, M. R. Surgical Treatment of Arteriosclerotic Aneurysms of the Abdominal Aorta. *A.M.A. Arch. Surg.* 64:307-319, 1952.

114. DETAKATS, G. Anticoagulant Therapy. *Surgery* 34:985-1004, 1953.

115. DETERLING, R. A., JR. Factors Influencing the Behavior of Synthetic Prostheses in the Vascular System. *Transpl. Bull.* 3:125-127, 1956.

116. ———. Discussion of paper by Lord, J. W., and Stone, P. W., "Use of Autologous Venous Grafts in the Peripheral Arterial System." *A.M.A. Arch. Surg.* 74:71-79, 1957.

117. ———. Cited by Weslowski, S. A., and Sauvage, L. R. "Heterologous Aortic Grafts—With Special Reference to Recipient Site, Ethylene Oxide Freeze-dry Preparation and Species of Origin." *Ann. Surg.* 145:187-198, 1957.

118. ———. Experience with Permanent By-pass Grafts in Treatment of Occlusive Arterial Disease. *A.M.A. Arch. Surg.* 76:247-260, 1958.

119. DETERLING, R. A., JR., and BHONSLAY, S. B. Use of Vessel Grafts and Plastic Prostheses for Relief of Superior Vena Caval Obstruction. *Surgery* 38:1008-1026, 1955.

120. ———. An Appraisal of Woven Synthetic Prostheses in the Vascular System *A.M.A. Arch. Surg.* 72:76-91. 1956.

121. DETERLING, R. A., JR., COLEMAN, C. C., JR., and PARSHLEY, M. S. Experimental Studies of the Frozen Homologous Aortic Graft. *Surgery* 29:419-440, 1951.

122. DETERLING, R. A., JR., and BHONSLAY, S. B. An Evaluation of Synthetic Materials and Fabrics Suitable for Blood Vessel Replacement. *Surgery* 38:71-89, 1955.

123. Diaz Sarasola, R. Un caso de Operación de San Mártin. (Contribución a la Casuistica). *Arch. cardiol. y hemat.* 10:137-143, 1929.

124. Dickinson, P. H. The Suitability of Skin as a Strengthening Material for Vein Grafts: An Experimental Study. *Brit. J. Surg.* 44:529-537, 1957.

125. Donovan, T. J. The Use of Plastic Tubes in the Reparative Surgery of Battle Injuries to Arteries With and Without Intra-Arterial Heparin Administration. *Ann. Surg.* 130:1024-1043, 1949.

126. Doss, A. K., Thomac, H. C., and Bond, T. B. Renal Arteriography, its Clinical Value. *Texas J. Med.* 38:277-280, 1942.

127. dos Santos, J. C. Sur la Désobstruction des Thromboses Artérielles Anciennes. *Mem. Acad. chir.*, Par. 73:400-411, 1947.

128. dos Santos, R., Lamas, A., and Pereira, C. J. L'Arteriographie des Membres de L'Aorte et ses Brances Abdominales. *Bull. Soc. nat. chir.*, Par. 55:587-601, 1929.

129. dos Santos, R., Lamas, A., and Caldas, J. P. *Artériographie des Membres et de l'Aorte Abdominale: Préface du Leriche.* Masson & Cie, pp. 192, 1931.

130. Dubost, C., Allary, M., and Oeconomos, N. A Propos du Traitement des Anévrysmes de l'Aorte. Ablation de l'Anévrysme Rétablissment de la Continuité par Greffe d'Aorte Humaine Conservée. *Mem. Acad. chir.*, Par. 77:381-383, 1951.

131. ———. Resection of an Aneurysm of the Abdominal Aorta. *A.M.A. Arch. Surg.* 64:405-408, 1952.

132. Dye, W. S., Grove, W. J., Olwin, J. H., and Julian, O. C. Two- to Four-Year Behavior of Vein Grafts in Lower Extremities. *A.M.A. Arch. Surg.* 72:64-68, 1956.

133. Dye, W. S., Olwin, J. H., and Julian, O. C. Further Considerations on the Indications for and Limitations of Direct Surgery in Arteriosclerosis. *Circulation*, N.Y. 8:708-714, 1953.

134. Eastcott, H. H. G. Arterial Grafting for the Ischaemic Lower Limb. *Ann. R. Coll. Surgeons*, England 13:177-198, 1953.

135. Eastcott, H. H. G., Holt, L. B., Peacock, J. H., and Rob, C. G. Preservation of Arterial Grafts by Freeze-Drying: A Simplified Method. *Lancet*, Lond. 266:1311-1314, 1954.

136. Eastcott, H. H. G., and Hufnagel, C. A. The Preservation of Arterial Grafts by Freezing. *Surg. Forum* 1:269-282, 1950.

137. Edwards, W. S. *Plastic Arterial Grafts.* C. C. Thomas, Springfield, Ill., 1957, pp. 126.

138. ———. Progress in Synthetic Graft Development—An Improved Crimped Graft of Teflon. *Surgery* 45:298-309, 1959.

139. Edwards, W. S., and Tapp, J. S. Chemically Treated Nylon Tubes as Arterial Grafts. *Surgery* 38:61-70, 1955.

140. ———. Peripheral Artery Replacement and Chemically Treated Nylon Tubes. *Surg. Gyn. Obst.* 102:443-449, 1956.

141. ———. A Flexible Aortic Bifurcation Graft of Chemically Treated Nylon. *Surgery* 41:723-728, 1957.

142. Egdahl, R. H. Silicone Rubber as Grafting Material. *A.M.A. Arch. Surg.* 71:694-696, 1955.

143. Egdahl, R. H., and Hume, D. M. Nonsuture Blood-Vessel Anastomosis: An Experimental Study Using Polyethylene as Prosthetic Material. *A.M.A. Arch. Surg.* 72:232-240, 1956.

144. Egdahl, R. H., Hume, D. M., and Schlang, H. A. Plastic Venous Prostheses. *Surg. Forum* 5:235-241, 1954.

145. Estes, J. E., Jr. Abdominal Aortic Aneurysm: A Study of 102 Cases. *Circulation,* N.Y. 2:258-264, 1950.

146. Etheredge, S. N., Yee, J., Smith, J. V., Schonberger, S., and Goldman, M. J. Successful Resection of a Large Aneurysm of the Upper Abdominal Aorta and Replacement with Homograft. *Surgery* 38:1071-1081, 1955.

147. Fariñas, P. L. A New Technique for the Arteriographic Examination of the Abdominal Aorta and its Branches. *Am. J. Roentg.* 46:641-645, 1941.

148. Farrar, T., and Sanders, R. L. The Diagnosis of Perforating Arteriosclerotic Abdominal Aortic Aneurysms: A Review of Cases. *Am. Surgeon* 22:623-629, 1956.

149. Fisher, B. Personal Experience.

150. Fisher, B., Adams, C., Wilde, R., and Fisher, E. R. The Sterilization and Storage of Lyophilized Blood Vessels. *Ann. Surg.* 143:73-80, 1956.

151. Fisher, B., Rosencrans, D., Adams, C., and Fisher, E. R. The Fate of Autogenous Skin Tubes as Aorta Grafts. *Surg. Gyn. Obst.* 102:309-314, 1956.

152. Fisher, B., Russ, C., Fedor, E. J., Wilde, R., Engstrom, P., and Fisher, E. R. Further Experimental Observations on Animals with Arterialized Livers. *Surgery* 38:181-193, 1955.

153. Fisher, B., Russ, C., Updegraff, H., and Fisher, E. R. Effect of Increased Hepatic Blood Flow Upon Liver Regeneration. *A.M.A. Arch. Surg.* 69:263-272, 1954.

154. Fisher, B., Wilde, R., Engstrom, P., and Fisher, E. R. Experimental Reconstruction of the Aortic Bifurcation. *Surgery* 39:940-949, 1956.

155. Fisher, E. R., and Fisher, B. The Effect of Induced Arteriosclerosis on Fresh and Lyophilized Aortic Homografts in the Rabbit. *Surgery* 40:530-542, 1956.

156. Flosdorf, E. W., and Mudd, S. Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances. *J. Immun.* 29:389-425, 1935.

157. Fontaine, R. Cited by Malan, E., "Treatment of Chronic Obliterative Arterial Disease with Venous Autografts." *Boll. Soc. piemont, chir.* 22:705, 1952.

158. Fontaine, R., Buck, P., Riveaux, R., Kim, M., and Hubinot, J. Treatment of Arterial Occlusion, Comparative Value of Thrombectomy, Thromboendarterectomy, Arteriovenous Shunt and Vascular Grafts (Fresh Venous Autografts). *Lyon chir.* 46:73-94, 1951.

159. Fontaine, R., Kim, M., and Kieny, R. Contribution Experiméntale l'Etude Biologique des Greffes Vascularies: Essai de Production d'un Autogreffon Conjonctif Tubulaire. *Presse méd.* 16:1791-1793, 1953.

160. Fontaine, R., Riveaux, R., Kim, M., and Kieny, R. Le Traitement Chirurgical des Oblitérations Artérielles Chroniquees des Membres. ler Congres de la Societe Europeenere de Chirurgia Cardio-vasculaire. 1:223, 1952.

161. Forssmann, W. Die Sondierung des Rechten Herzens. *Klin. Wschr.* 2:2085-2087, 1929.

162. Foster, J. H., Lance, E. M., and Scott, H. W., Jr. Experience With Ethylene Oxide Treated Freeze-dry Arterial Homografts in 110 Consecutive Patients. *Ann. Surg.* 148:230-238, 1958.

163. Freeman, N. E., and Gilfillan, R. S. Regional Heparinization After Thromboendarterectomy in the Treatment of Obliterative Arterial Disease: Preliminary Report Based on 12 Cases. *Surgery* 31:115-131, 1952.

164. FREEMAN, N. E., and NICHOLSON, G. J. Evaluation of Thromboendarterectomy in Treatment of Obliterative Arterial Disease. *A.M.A. Arch. Surg.* 78:280-287, 1959.

165. FREEMAN, N. E., WYLIE, E. J., and GILFILLAN, R. S. Regional Heparinization in Vascular Surgery. *Surg. Gyn. Obst.* 90:406-412, 1950.

166. GASPAR, M. R. Failure and Replacement of Abdominal Aortic Grafts. *Am. J. Surg.* 96:202-212, 1958.

167. GASS, H. H., and SMATHERS, H. M. Carotid Artery Insufficiency Corrected by Internal Carotid Thrombectomy. *Neurology* 7:670-672, 1957.

168. GAUTHIER-VILLARS, P., and OUDOT, J. Greffe Vasculaire Hétérogène (Etude Expérimentale). *Presse méd.* 58:667-668, 1950.

169. GERBODE, F. Ruptured Aortic Aneurysm: A Surgical Emergency. Editorial *Surg. Gyn. Obst.* 98:759, 1954.

170. GERBODE, F., BRAIMBRIDGE, M., OSBORN, J. J., HOOD, M., and FRENCH, S. Traumatic Thoracic Aneurysms: Treatment by Resection and Grafting With the Use of an Extracorporeal By-pass. *Surgery* 42:975-985, 1957.

171. GIRVIN, G. W., SCHLOSSER, R. J., EADE, G. G., and MERENDINO, K. A. Teflon Fabric Grafts in Growing Pigs. *Surgery* 42:710-716, 1957.

172. GLENN, F., KEEFER, E. B. C., DOTTER, C. T., and BEAL, J. M. Observations on Experimental Aortic Anastomosis. *Proc. Soc. Exp. Biol.*, N.Y. 71:619-622, 1949.

173. GLIEDMAN, M. L., AYERS, W. B., and VESTAL, B. L. Aneurysms of the Abdominal Aorta and Its Branches—A Study of Untreated Patients. *Ann. Surg.* 146:207-214, 1957.

174. GOETZ, R. H. A Continuous Interrupted Everting Suture for Arterial Surgery. *Surg. Gyn. Obst.* 101:245-246, 1955.

175. GOODMAN, C. Arteriovenous Anastomosis of the Femoral Vessels for Impending Gangrene. *Ann. Surg.* 60:62-87, 1914.

176. ———. Suture of Blood-Vessel Injuries from Projectiles of War. *Surg. Gyn. Obst.* 27:528-529, 1918.

177. ———. *Surgery of the Heart; Blood Vessels; Thrombosis and Embolism and Blood Transfusion.* Bruxelles, M. Hayez, 1920, pp. 58.

178. ———. Suture Repair of War Injuries to the Blood Vessels. *J. Internat. Coll. Surgeons* 6:127-132, 1943.

179. GRAHAM, A. J. P. Arterial Homografts: An Experimental Study. *Guy's Hosp. Rep.*, Lond. 101:186-206, 1952.

180. GRIFFITH, C. A., EADE, G. G., ZECH, R. K., and HARKINS, H. N. A New Technique for Compilation Arterial Grafts: Vinyon® "N" Cloth Supplemented With a Longitudinal Autogenous Arterial Strip. *Surg. Gyn. Obst.* 101:225-234, 1955.

181. GRINDLAY, J. H., and WAUGH, J. M. Plastic Sponge Which Acts as a Framework for Living Tissue. Experimental Studies and Preliminary Report of Use to Reinforce Abdominal Aneurysms. *A.M.A. Arch. Surg.* 63:288-297, 1951.

182. GROSS, R. E. Complete Surgical Division of the Patent Ductus Arteriosus. A Report of Fourteen Successful Cases. *Surg. Gyn. Obst.* 78:36-43, 1944.

183. ———. Surgical Correction for Coarctation of the Aorta. *Surgery* 18:673-678, 1945.

184. GROSS, R. E., HURWITT, E. S., BILL, A. H., JR., and PEIRCE, E. C., II. Methods for Preservation and Transplantation of Arterial Grafts: Observations on Arterial Grafts in Dogs: Report of Transplantation of Preserved Arterial Grafts in Nine Human Cases. *Surg. Gyn. Obst.* 88:689-701, 1949.

185. GROSS, R. E., and HUBBARD, J. P. Surgical Ligation of a Patent Ductus Arteriosus. Report of First Successful Case. *J. Am. M. Ass.* 112:729-731, 1939.

186. GROSS, R. E., and HUFNAGEL, C. A. Coarctation of the Aorta—Experimental Studies Regarding its Surgical Correction. *N. England J. M.* 233:287-293, 1945.

187. GROSS, R. E., HURWITT, E. S., BILL, A. H., JR., and PEIRCE, E. C., II. Preliminary Observations on the Use of Human Arterial Grafts in the Treatment of Certain Cardiovascular Defects. *N. England J. M.* 239:578-579, 1948.

188. GURDJIAN, E. S., and WEBSTER, J. E. Thrombo-Endarterectomy of the Carotid Bifurcation and the Internal Carotid Artery. *Surg. Gyn. Obst.* 106:421-426, 1958.

189. GUTHRIE, C. C. Heterotransplantations of Blood Vessels. *Am. J. Physiol.* 19:482-487, 1907.

190. ———. Transplantation of Formaldehyde-Fixed Blood Vessels. *Science* 27:473, 1908.

191. GWATHMEY, O., and THOMPSON, C. W. Aneurysm Formation in a Homologous Aortic Graft in a Human: Report of a Case. *J. Thorac. Surg.* 30:218-229, 1955.

192. HAIMOVICI, H., MAIER, N., and STRAUSS, L. Fate of Aortic Homografts in Experimental Canine Atherosclerosis. *A.M.A. Arch. Surg.* 76:282-288, 1958.

193. HALLÉN, L. G. Methods of Preservation and Fate of Homologous Arterial Grafts: An Experimental Study in Dogs. *Acta. chir. scand.*, supp. 204:1-67, 1955.

194. HAMBLIN, R. G., and LORD, J. W., JR. Fatal Rupture of a Preserved Aortic Homograft. *J. Am. M. Ass.* 155:1406-1407, 1954.

195. HAMMER, J. M., SEAY, P. H., DEGROAT, A., and PRUST, F. W. Preserving Arterial Segments for the Blood Vessel Bank. *A.M.A. Arch. Surg.* 69:97-100, 1954.

196. HANLON, R. Reconstruction of the Superior Vena Cava. Moving Picture, American College of Surgeons.

197. HARDIN, C. A. Orlon and Nylon Prostheses for Abdominal Aneurysm and a Five Year Observation on Experimental Aortic Homografts. *Ann. Surg.* 146:78-85, 1957.

198. HARDY, J. D. Ruptured Aneurysm of Abdominal Aorta: Successful Resection and Homografting Five Days After Initial Hemorrhage. *Mississippi Doctor* 34:119-120, 1956.

199. HARE, H. A. Treatment of Aortic Aneurysm by Wiring and Electrolysis. *J. Am. M. Ass.* 76:587-588, 1921.

200. HARRIS, E. J., SHUMACKER, H. B., JR., SIDERYS, H., MOORE, T. C., and GRICE, P. F. Pliable Plastic Aortic Grafts. Experimental Comparison of a Number of Materials. *A.M.A. Arch. Surg.* 71:449-459, 1955.

201. HARRISON, J. H. The Use of Teflon as a Blood Vessel Replacement in Experimental Animals. *Surg. Gyn. Obst.* 104:81-87, 1957.

202. ———. Synthetic Materials as Vascular Prostheses. I. A Comparative Study in Small Vessels of Nylon, Dacron, Orlon, Ivalon Sponge and Teflon. *Am. J. Surg.* 95:3-15, 1958.

203. ———. Synthetic Materials as Vascular Prostheses. II. A Comparative Study of Nylon, Dacron, Orlon, Ivalon Sponge and Teflon in Large Blood Vessels with Tensile Strength Studies. *Am. J. Surg.* 95:16-24, 1958.

204. HARRISON, J. H., and ADLER, R. H. Nylon as a Vascular Prosthesis in Experimental Animals with Tensile Strength Studies. *Surg. Gyn. Obst.* 103:613-617, 1956.

205. HEINZEN, B. R., DUNBAR, H. S., and PARSONS, H. Thrombosis of Abdominal Aorta and Iliac Arteries. *Ann. Surg.* 139:148-157, 1954.

206. HELMSWORTH, J. A., MCGUIRE, J., FELSON, B., and SCOTT, R. C. Visualization of Coronary Arteries During Life. *Circulation*, N.Y. 3:282-288, 1951.

207. HENLINE, R. B., and MOORE, S. W. Renal Arteriography—Preliminary Report of Experimental Study. *Am. J. Surg.* 32:222-229, 1936.

208. HENROTIN, E., and VEROFT, R. Greffes Vascularies et Banque d'Artéres; Etude Experiméntale. *Acta chir. belg.* 52:175-194, 1953.

209. HENSON, G. F., and ROBB, C. G. A Comparative Study of the Effects of Different Arterial Clamps on the Vessel Wall. *Brit. J. Surg.* 43:561-564, 1956.

210. HERRMANN, L. G., and BOLLACK, C. Arteriogenesis Induced by Tubes of Plastic Mesh. *Surgery* 38:993-998, 1955.

211. HIERTONN, T., and BORG, T. Arterial Transplantation from Blood Vessel Bank. *Nord. med.* 44:1387-1389, 1950.

212. HOLMAN, C. W., and STEINBERG, I. Treatment of Superior Vena Caval Occlusion by Arterial Graft: Preliminary Report. *J. Am. M. Ass.* 155:1403-1405, 1954.

213. HOLMAN, E. The Physiology of an Arteriovenous Fistula. *A.M.A. Arch. Surg.* 7:64-82, 1923.

214. ———. Experimental Studies in Arteriovenous Fistulas. I. Blood Volume Variations. *A.M.A. Arch. Surg.* 9:822-836, 1924.

215. ———. Experimental Studies in Arteriovenous Fistulas. II. Pulse and Blood Pressure Variations. *A.M.A. Arch. Surg.* 9:837-855, 1924.

216. ———. Experimental Studies in Arteriovenous Fistulas. III. Cardiac Dilitation and Blood Vessel Changes. *A.M.A. Arch. Surg.* 9:856-879, 1924.

217. ———. Observations on the Surgery of the Large Arteries. *Ann. Surg.* 85:173-184, 1927.

218. HOPFNER, E. Über Gefässnaht, Gefässtransplantationen und Replantation von Amputirten Extremitäten. *Arch. klin. chir.* 70:417-471, 1903.

219. HORSLEY, J. S. Operative Treatment for Threatened Gangrene of the Foot, With Special Reference to Reversal of the Circulation. *J. Am. M. Ass.* 67:492-499, 1916.

220. HORSLEY, J. S. Suturing Blood Vessels. *J. Am. M. Ass.* 77:117-121, 1921.

221. HORSLEY, J. S., and WHITEHEAD, R. H. A Study of Reversal of the Circulation in the Lower Extremity. *J. Am. M. Ass.* 64:873-877, 1915.

222. HOTZ, G. Zur Chirurgie der Blutgefässe. *Beitr. klin. chir.* 97:177-188, 1915.

223. HOWELL, W. H., and HOLT, E. Two New Factors in Blood Coagulation—Heparin and Pro-Antithrombin. *Am. J. Physiol.* 47:328-341, 1918.

224. HOYE, S. J., and WARREN, R. Follow-up Studies of Iliofemoral Arterial Reconstruction in Arteriosclerosis Obliterans. *N. England J. M.* 254:102-106, 1956.

225. HUFNAGEL, C. A. Permanent Intubation of the Thoracic Aorta. *A.M.A. Arch. Surg.* 54:382-389, 1947.

226. ———. Preserved Homologous Arterial Transplants. *Bull. Am. Coll. Surgeons* 32:231, 1947.

227. ———. The Use of Rigid and Flexible Plastic Prostheses for Arterial Replacement. *Surgery* 37:165-174, 1955.

228. HUFNAGEL, C. A., and RABIL, P. Replacement of Arterial Segments, Utilizing Flexible Orlon Prostheses. *A.M.A. Arch. Surg.* 70:105-110, 1955.

229. Hufnagel, C. A., Rabil, P. J., and Reed, L. A Method for the Preservation of Arterial Homo- and Heterografts. *Surg. Forum* 4:162-168, 1953.

230. Hui, K. K. L., Keefer, E. B. C., Deterling, R. A., Jr., Parshley, M. S., Humphreys, G. H., and Glenn, F. Early Results of Experimental Studies of the Action of High Intensity Electrons on Aortic Homografts. *Surg. Forum* 2:255-261, 1951.

231. Humphries, A. W., deWolfe, V. G., and LeFevre, F. A. Major Arterial Grafting in 169 Consecutive Cases. *A.M.A. Arch. Surg.* 74:65-70, 1957.

232. Hurwitt, E. S., Seidenberg, B., Fell, S. C., and Abelson, D. S. Resection of Aneurysm of Thoracoabdominal Aorta: Involvement of Celiac and Superior Mesenteric Arteries, With Rupture Into Psoas Muscle. *A.M.A. Arch. Surg.* 76:239-246, 1958.

233. Hyatt, G. W., Turner, T. C., Bassett, C. A. L., Pate, J. W., and Sawyer, P. N. New Methods for Preserving Bone, Skin and Blood Vessels. *Postgrad. M.* 12:239-254, 1952.

234. Inokuchi, K. A New Type of Blood Vessel Suturing Apparatus. *A.M.A. Arch. Surg.* 77:954-957, 1958.

235. Inui, F. K., Shannon, J., and Howard, J. M. Arterial Injuries in the Korean Conflict—Experiences with 111 Consecutive Injuries. *Surgery* 37:850-857, 1955.

236. Jacobson, W. H. A. *The Operations of Surgery.* 6th Edition by R. P. Rowlands and Phillip Turner. J. & A. Churchill, London, 1915, 1, 843, 894.

237. Jahnke, E. J., Jr., and Seeley, S. F. Acute Vascular Injuries in the Korean War: Analysis of 77 Consecutive Cases. *Ann. Surg.* 138:158-177, 1953.

238. Jamplis, R. W., Rugtiv, G. M., Burkman, V., and Cressman, R. D. Resection of Ruptured Abdominal Aortic Aneurysm with Fatal Rupture of Aortic Homograft. *Ann. Surg.* 147:393-398, 1958.

239. Javid, H., Dye, W. S., Grove, W. J., and Julian, O. C. Resection of Ruptured Aneurysms of the Abdominal Aorta. *Ann. Surg.* 142:613-623, 1955.

240. Jesseph, J. E., Stevenson, J. K., and Harkins, H. N. Arterial Grafts of Compressed Polyvinyl Alcohol. (Ivalon) Sponge, An Experimental Study. *West J. Surg.* 64:70-75, 1956.

241. Johnson, J., Kirby, C. K., Allam, M. W., and Hagan, W. The Growth of Vascular Anastomoses with Continuous Posterior and Interrupted Anterior Silk Sutures. *Surgery* 29:721-725, 1951.

242. Johnson, J., Kirby, C. K., Allam, M. W., and Hagan, W. The Growth of Vena Cava and Aorta Grafts. *Surgery* 29:726-730, 1951.

243. Johnson, J., Kirby, C. K., Greifenstein, F. E., and Castillo, A. The Experimental and Clinical Use of Vein Grafts to Replace Defects of Large Arteries. *Surgery* 26:945-956, 1949.

244. Johnson, J., Kirby, C. K., and Hardy, J. D. Aneurysm Formation in Experimental Vein Grafts in the Thoracic Aorta. *Surgery* 33:207-212, 1953.

245. Jones, T. I., and Dale, W. A. Study of Peripheral Autogenous Vein Grafts. *A.M.A. Arch. Surg.* 76:294-309, 1958.

246. Jordan, G. L., Jr., DeBakey, M. E., and Halpert, B. Lipid Changes Produced by Chronic Hypercholesterolemia in Nylon and Orlon Replacements of Canine Thoracic Aorta. *Proc. Soc. Exp. Biol., N. Y.* 99:484-487, 1958.

247. Jordan, P. Arteriovenous Shunts for Revascularization of Ischemic [illegible] *J. Michigan M. Soc.* 48:1011-1012, 1949.

248. Jordan, P., Jr., Huertons, T., and Johnston, C. G. Arterial Repl[illegible] in Trauma. *Am. J. Surg.* 85:424-430, 1953.

249. JORDAN, P., and JOHNSTON, C. G. The Use of Arterio-venous Shunts in Ischemic Limbs. *Proc. of 13th Congress of International Soc. of Surgery*, New Orleans, Oct. 10, 1949.

250. JULIAN, O. C., DETERLING, R. A., JR., DYE, W. S., BHONSLAY, S., GROVE, W. J., BELIO, M. L., and JAVID, H. Dacron Tube and Bifurcation Arterial Prostheses Produced to Specification. *II. Continued Clinical Use and the Addition of Microcrimping. A.M.A. Arch. Surg.* 78:260-270, 1959.

251. JULIAN, O. C., DETERLING, R. A., JR., SU, H. H., DYE, W. S., and BELIO, M. L. Dacron Tube and Bifurcation Arterial Prostheses Produced to Specification. *Surgery* 41:50-61, 1957.

252. JULIAN, O. C., DYE, W. S., OLWIN, J. H., and JORDAN, P. H. Direct Surgery of Arteriosclerosis. *Ann. Surg.* 136:459-474, 1952.

253. JULIAN, O. C., GROVE, W. J., DYE, W. S., OLWIN, J., and SADOVE, M. S. Direct Surgery of Arteriosclerosis: Resection of Abdominal Aorta With Homologous Aortic Graft Replacement. *Ann. Surg.* 138:387-403, 1953.

254. *JULIAN, O. C., GROVE, W. J., and NORBERG, C. A. Techniques in Arterial* Surgery. *Surgery* 36:161-170, 1954.

255. KAMPMEIER, R. H. Aneurysm of Abdominal Aorta: Study of 73 Cases. *Am. J. M. Sc.* 192:97-109, 1936.

256. KANAR, E. A., NYHUS, L. M., SCHMITZ, E. J., SAUVAGE, L. R., MOORE, H. G., JR., ZECH, R. K., and HARKINS, H. N. Differential Behavior of Arterial Homografts Implanted in the Thoracic and Abdominal Aorta. *J. Thorac. Surg.* 28:310-319, 1954.

257. KANAR, E. A., SCHMITZ, E. J., SAUVAGE, L. R., NYHUS, L. M., MOORE, H. G., JR., MERENDINO, K. A., and HARKINS, H. N. Experimental Vascular Grafts. I. The Effects of Dicetyl Phosphate on Venous Autografts Implanted in the Thoracic Aorta of Growing Pigs: A Preliminary Report. *Ann. Surg.* 138:73-81, 1953.

258. KAY, E. B. Discussion of paper by Scannell, J. G. and Shaw, R. S., "Surgical Reconstruction of the Superior Vena Cava." *J. Thorac. Surg.* 28:163-174, 1954.

259. KEEFER, E. B. C., GLENN, F., and DOTTER, C. T. Two Year Postoperative Study of Thoracic Arterial Grafts Into Puppies. *Surg. Forum* 3:140-147, 1952.

260. KIEHN, C. L., BENSON, J., GLOVER, D. M., and BERG, M. Study of Revascularization of Blood Vessel Grafts by Means of Radioactive Phosphorus. *A.M.A. Arch. Surg.* 65:477-486, 1952.

261. KIMOTO, S., SUGIE, S., and TSUNODA, M. Experimental and Clinical Studies on Arterial Homo and Heterografts Preserved in Alcohol. Primary Report. *A.M.A. Arch. Surg.* 69:549-563, 1954.

262. KINCAID, O. W., and DAVIS, G. D. Abdominal Aortography. *N. England J. M.* 259:1017-1024 and 1067-1073, 1958.

263. KITTLE, C. F., and TAQUECHEL, C. A Preliminary Investigation of Dermal Heterografts (Leather) as Prostheses for Vascular Defects. *A.M.A. Arch. Surg.* 74:96-104, 1957.

264. KLASSEN, K. P., ANDREWS, N. C., and CURTIS, G. M. Diagnosis and Treatment of Superior-Vena-Cava Obstruction. *A.M.A. Arch. Surg.* 63:311-325, 1951.

265. KLOTZ, O., PERMAR, H. H., and GUTHRIE, C. C. End Results of Arterial Transplants. *Ann. Surg.* 78:305-320, 1923.

266. KNOX, G., and WEST, J. P. Dacron Grafts in Treatment of Arteriosclerotic Occlusion of Superficial *Femoral Artery (Report of Seven Cases). Ann. Surg.* 145:59-67, 1957.

267. Kremer, K. Probleme der Freien Gafässtransplantation: Konservierungsemethoden zur Aufbewahrung von Gefästransplantaten. *Zbl. Chir.* 78:1857-1867, 1953.

268. Kremer, K., Volkmann, E., Francke, D., and Suchowsky, G. The Problem of Transplantation of Blood Vessels; Experimental Studies of Autoplastic Vein Transplantation. *Arch. klin. Chir.* 277:471-482, 1953.

269. Kuetgens, G., and Schlicht, L. Ein Beitrag zur Frage der Konservierung und Transplantation von Aortenstücken. *Müchen. med. Wchnschr.* 94:1181-1182, 1952.

270. Kunlin, J. Le Traitement de Líschémie Artéritique par la Greffe Veineuse Longue. *Rev. chir.*, Paris 70:206-236, 1951.

271. Lam, C. R., and Aram, H. H. Resection of the Descending Thoracic Aorta for Aneurysm. A Report of the Use of a Homograft in a Case and an Experimental Study. *Ann. Surg.* 134:743-752, 1951.

272. Lary, B. G., Meine, E. L., and deTakats, G. The Experimental Use of Steel Mesh Tubes for Replacement of Arterial Segments. *A.M.A. Arch. Surg.* 72:69-75, 1956.

273. Laufman, H., and Heller, R. E. The Effect of Heparin on Wound Healing. *Surg. Gyn. Obst.* 76:655-658, 1943.

274. Laufman, H., Hohf, R., Bernhard, V., and Trippel, O. End-to-Side By-Pass Homograft Without Resection in Segmental Arterial Occlusion. *A.M.A. Arch. Surg.* 73:418-431, 1956.

275. Lawrence, G. H. Successful Nylon Prosthesis for the Femoral Artery and Vein. *A.M.A. Arch. Surg.* 75:785-787, 1957.

276. Lazzarini, A. A. Cited by Wesolowski, S. A. and Sauvage, L. R.: "Heterologous Aortic Grafts—With Special Reference to Recipient Site, Ethylene Oxide Freeze-Dry Preparation and Species of Origin." *Ann. Surg.* 145:187-198, 1957.

277. LeDentu, J. F. A., and Delbet, P. *Nouveau Traité de Chirurgie.* II. Affections Chirurgicales des Artèrés. 94 Paris, 1911.

278. Leger, L. Essais de Revascularisation d'un Membre Paranastomose. Artério-Veineuse Termino-Terminale. *Presse méd.* 57:1198-1200, 1949.

279. ———. La Conservation des Greffons Artériels dans le Formol. *Presse méd.* 61:1562, 1953.

280. Leger, L., and Oudot, J. Greffe Artérielle Hétérogène. *Mém. Acad. chir.*, Par. 76:728-730, 1950.

281. Lehr, H. B., and Blakemore, W. S. Arterial Homografts, with a Presentation of 84 cases. *Surg. Gyn. Obst.* 105:209-232, 1957.

282. Lehr, H. B., Blakemore, W. S., Sawyer, P. N., Glauser, F., and Johnson, J. An Apparatus for the Preparation of Homologous Arterial Grafts by Freeze-Drying. *Surgery* 37:576-584, 1955.

283. Leriche, R. Des Oblitérations Artérielles Hautes (Oblitération de la Terminaison de l'Aorte) Comme Causes des Insuffisances Circulatoires des Membres Inférieurs. *Bull. et mém. Soc. Chir.*, Paris 49:1404-1406, 1923.

284. ———. De la Résection du Carrefour Aortico-Iliaque Avec Double Sympathectomie Lombaire pour Thrombose Artéritique de l'Aorte; le Syndrome de l'Obliteration Termino-Aortique par Artérite. *Presse méd*, 48:601-604, 1940.

285. Leriche, R., and Kunlin, J. Essais de Désobstruction des Artéres Thrombosées Suivant la Technique de Jean Cid dos Santos. *Lyon Chir.* 42:675-682, 1947.

286. Leriche, R., and Morel, A. The Syndrome of Thrombotic Obliteration of the Aortic Bifurcation. *Ann. Surg.* 127:193-206, 1948.

287. Levy, L. M., Hannon, D. W., Sprafka, J. L., and Baronofsky, I. D. A Method for Coronary Arteriography. *Ann. Surg.* 143:412-415, 1956.
288. Lexer, E. Die Ideale Operation des Arteriellen und des Arteriell-Venösen Aneurysma. *Arch. f. klin. Chir.* 83:459-477, 1907.
289. Lilienthal, H. Arteriovenous Anastomosis for Thrombo-Angiitis Obliterans. *Trans. Amer. Surg. Ass.* 58:279, 1914.
290. Lillihei, W. C. Personal communication to Edwards, W. S., "Plastic Arterial Grafts." C. T. Thomas, 1957, Springfield, Ill., pp. 126.
291. Lima, M. F. Estudôs Sobrê Enxertos Arteriais. *Rev. brasil cir.* 27:341-357, 1954.
292. Linton, R. R. Intrasaccular Wiring of Abdominalarteriosclerotic Aneurysms by the "Pack" Method. *Angiology* 2:485-498, 1951.
293. ———. Discussion of paper by DeBakey, M. E., Crawford, E. S., Cooley, D. A., and Morris, G. C., Jr., "Surgical Considerations of Occlusive Disease of *the Abdominal Aorta and Iliac and Femoral Arteries: Analysis of 803 Cases.*" *Ann. Surg.* 148:306-324, 1958.
294. ———. Discussion of paper by Wylie, E. J., and Goldman, L., "The Role of Aortography in the Determination of Operability in Arteriosclerosis of the Lower Extremities." *Ann. Surg.* 148:325-342, 1958.
295. ———. Discussion of paper by Freeman, N. E., and Nicholson, G. J., "Evaluation of Thromboendarterectomy in Treatment of Obliterative Arterial Disease." *A.M.A. Arch. Surg.* 78:280-287, 1959.
296. Linton, R. R., and Menendez, C. V. Arterial Homografts: A Comparison of Results with *End-to-End and End-to-Side Vascular Anastomoses. Ann Surg.* 142:568-585, 1955.
297. Littman, J. K., and Brodman, H. R. Surgery in the Presence of the Therapeutic Effect of Dicumarol. *Surg. Gyn. Obst.* 101:709-714, 1955.
298. LoGrippo, G. A., Overhulse, P. R., Szilagyi, D. E., and Hartman, F. W. Procedure for Sterilization of Arterial Homografts with Beta-Propiolactone. *Laborat. Invest.* 4:217-231, 1955.
299. Longmire, W. P., Jr., Cannon, J. A., and Kattus, A. A. Direct-Vision Coronary Endarterectomy for Angina Pectoris. *N. England J. M.* 259:993-999, 1958.
300. Lord, J. W., and Stone, P. W. Use of Autologous Venous Grafts in the Peripheral Arterial System. *A.M.A. Arch. Surg.* 74:71-79, 1957.
301. Lowenberg, E. L. Aneurysm of the Abdominal Aorta: Report of Two Cases Treated by "Cutis Grafting." *Angiology* 1:396-404, 1950.
302. Lozzi, V. L'Anastomosi Artero-Venosa Nella Chirurgia dei Grossi Vasi. *Rinasc. med.* 12:53-55, 1935.
303. Lund, J., and Lund, F. *Sterilization and Preservation of Arterial Homografts:* Experimental and Clinical Studies. *Acta. chir. scand.* 113:458-460, 1957.
304. Mahaffey, J. H. Ruptured Aneurysm of Abdominal Aorta in an Eighty-five-Year-Old Man: Successful Resection and Replacement by Orlon Prosthesis. *A.M.A. Arch. Surg.* 73:729-732, 1956.
305. Makins, G. H. On the Vascular Lesions Produced by Gunshot Injuries and Their Results. *Brit. J. Surg.* 3:353-421, 1916.
306. ———. Blessures des Vaisseaux. Comptes Rendus de la Conférence Chirgicale Interalliée pour l'Etude des Places de Guerre. *Arch. de med. et pharm. mil.* 68:341-348, 1917.
307. ———. The Hunterian Oration on the Influence Exerted by the Military Experience of John Hunter on Himself and the Military Surgeon of Today. *Lancet*, Lond. 1:249-254, 1917.

267. KREMER, K. Probleme der Freien Gafässtransplantation: Konservierungsemethoden zur Aufbewahrung von Gefästransplantaten. *Zbl. Chir.* 78:1857-1867, 1953.
268. KREMER, K., VOLKMANN, E., FRANCKE, D., and SUCHOWSKY, G. The Problem of Transplantation of Blood Vessels; Experimental Studies of Autoplastic Vein Transplantation. *Arch. klin. Chir.* 277:471-482, 1953.
269. KUETGENS, G., and SCHLICHT, L. Ein Beitrag zur Frage der Konservierung und Transplantation von Aortenstücken. *Müchen. med. Wchnschr.* 94:1181-1182, 1952.
270. KUNLIN, J. Le Traitement de Líschémie Artéritique par la Greffe Veineuse Longue. *Rev. chir.*, Paris 70:206-236, 1951.
271. LAM, C. R., and ARAM, H. H. Resection of the Descending Thoracic Aorta for Aneurysm. A Report of the Use of a Homograft in a Case and an Experimental Study. *Ann. Surg.* 134:743-752, 1951.
272. LARY, B. G., MEINE, E. L., and DETAKATS, G. The Experimental Use of Steel Mesh Tubes for Replacement of Arterial Segments. *A.M.A. Arch. Surg.* 72:69-75, 1956.
273. LAUFMAN, H., and HELLER, R. E. The Effect of Heparin on Wound Healing. *Surg. Gyn. Obst.* 76:655-658, 1943.
274. LAUFMAN, H., HOHF, R., BERNHARD, V., and TRIPPEL, O. End-to-Side By-Pass Homograft Without Resection in Segmental Arterial Occlusion. *A.M.A. Arch. Surg.* 73:418-431, 1956.
275. LAWRENCE, G. H. Successful Nylon Prosthesis for the Femoral Artery and Vein. *A.M.A. Arch. Surg.* 75:785-787, 1957.
276. LAZZARINI, A. A. Cited by Wesolowski, S. A. and Sauvage, L. R.: "Heterologous Aortic Grafts—With Special Reference to Recipient Site, Ethylene Oxide Freeze-Dry Preparation and Species of Origin." *Ann. Surg.* 145:187-198, 1957.
277. LEDENTU, J. F. A., and DELBET, P. *Nouveau Traité de Chirurgie.* II. Affections Chirurgicales des Artèrés. 94 Paris, 1911.
278. LEGER, L. Essais de Revascularisation d'un Membre Paranastomose. Artério-Veineuse Termino-Terminale. *Presse méd.* 57:1198-1200, 1949.
279. ———. La Conservation des Greffons Artériels dans le Formol. *Presse méd.* 61:1562, 1953.
280. LEGER, L., and OUDOT, J. Greffe Artérielle Hétérogène. *Mém. Acad. chir.*, Par. 76:728-730, 1950.
281. LEHR, H. B., and BLAKEMORE, W. S. Arterial Homografts, with a Presentation of 84 cases. *Surg. Gyn. Obst.* 105:209-232, 1957.
282. LEHR, H. B., BLAKEMORE, W. S., SAWYER, P. N., GLAUSER, F., and JOHNSON, J. An Apparatus for the Preparation of Homologous Arterial Grafts by Freeze-Drying. *Surgery* 37:576-584, 1955.
283. LERICHE, R. Des Oblitérations Artérielles Hautes (Oblitération de la Terminaison de l'Aorte) Comme Causes des Insuffisances Circulatoires des Membres Inférieurs. *Bull. et mém. Soc. Chir.*, Paris 49:1404-1406, 1923.
284. ———. De la Résection du Carrefour Aortico-Iliaque Avec Double Sympathectomie Lombaire pour Thrombose Artéritique de l'Aorte; le Syndrome de l'Oblitération Termino-Aortique par Artérite. *Presse méd*, 48:601-601, 1910.
285. LERICHE, R., and KUNLIN, J. Essais de Désobstruction des Artéres Thrombosées Suivant la Technique de Jean Cid dos Santos. *Lyon Chir.* 42:675-682, 1947.
286. LERICHE, R., and MOREL, A. The Syndrome of Thrombotic Obliteration of the Aortic Bifurcation. *Ann. Surg.* 127:193-206, 1948.

287. LEVY, L. M., HANNON, D. W., SPRAFKA, J. L., and BARONOFSKY, I. D. A Method for Coronary Arteriography. *Ann. Surg.* 143:412-415, 1956.

288. LEXER, E. Die Ideale Operation des Arteriellen und des Arteriell-Venösen Aneurysma. *Arch. f. klin. Chir.* 83:459-477, 1907.

289. LILIENTHAL, H. Arteriovenous Anastomosis for Thrombo-Angiitis Obliterans. *Trans. Amer. Surg. Ass. 58:279, 1914.*

290. LILLIHEI, W. C. Personal communication to Edwards, W. S., "Plastic Arterial Grafts." C. T. Thomas, 1957, Springfield, Ill., pp. 126.

291. LIMA, M. F. Estudōs Sobrê Enxertos Arteriais. *Rev. brasil cir.* 27:311-357, 1954.

292. LINTON, R. R. Intrasaccular Wiring of Abdominalarteriosclerotic Aneurysms by the "Pack" Method. *Angiology* 2:485-498, 1951.

293. ———. Discussion of paper by DeBakey, M. E., Crawford, E. S., Cooley, D. A., and Morris, G. C., Jr., "Surgical Considerations of Occlusive Disease of the Abdominal Aorta and Iliac and Femoral Arteries: Analysis of 803 Cases." *Ann. Surg.* 148:306-324, 1958.

294. ———. Discussion of paper by Wylie, E. J., and Goldman, L., "The Role of Aortography in the Determination of Operability in Arteriosclerosis of the Lower Extremities." *Ann. Surg.* 148:325-342, 1958.

295. ———. Discussion of paper by Freeman, N. E., and Nicholson, G. J., "Evaluation of Thromboendarterectomy in Treatment of Obliterative Arterial Disease." *A.M.A. Arch. Surg.* 78:280-287, 1959.

296. LINTON, R. R., and MENENDEZ, C. V. Arterial Homografts: A Comparison of Results with End-to-End and End-to-Side Vascular Anastomoses. *Ann Surg.* 142:568-585, 1955.

297. LITTMAN, J. K., and BRODMAN, H. R. Surgery in the Presence of the Therapeutic Effect of Dicumarol. *Surg. Gyn. Obst.* 101:709-714, 1955.

298. LOGRIPPO, G. A., OVERHULSE, P. R., SZILAGYI, D. E., and HARTMAN, F. W. Procedure for Sterilization of Arterial Homografts with Beta-Propiolactone. *Laborat. Invest.* 4:217-231, 1955.

299. LONGMIRE, W. P., JR., CANNON, J. A., and KATTUS, A. A. Direct-Vision Coronary Endarterectomy for Angina Pectoris. *N. England J. M.* 259:993-999, 1958.

300. LORD, J. W., and STONE, P. W. Use of Autologous Venous Grafts in the Peripheral Arterial System. *A.M.A. Arch. Surg.* 74:71-79, 1957.

301. LOWENBERG, E. L. Aneurysm of the Abdominal Aorta: Report of Two Cases Treated by "Cutis Grafting." *Angiology* 1:396-404, 1950.

302. LOZZI, V. L'Anastomosi Artero-Venosa Nella Chirurgia dei Grossi Vasi. *Rinasc. med.* 12:53-55, 1935.

303. LUND, J., and LUND, F. Sterilization and Preservation of Arterial Homografts: Experimental and Clinical Studies. *Acta. chir. scand.* 113:458-460, 1957.

304. MAHAFFEY, J. H. Ruptured Aneurysm of Abdominal Aorta in an Eighty-five-Year-Old Man: Successful Resection and Replacement by Orlon Prosthesis. *A.M.A. Arch. Surg.* 73:729-732, 1956.

305. MAKINS, G. H. On the Vascular Lesions Produced by Gunshot Injuries and Their Results. *Brit. J. Surg.* 3:353-421, 1916.

306. ———. Blessures des Vaisseaux. Comptes Rendus de la Conférence Chirgicale Interalliée pour l'Etude des Places de Guerre. *Arch. de med. et pharm. mil.* 68:341-348, 1917.

307. ———. The Hunterian Oration on the Influence Exerted by the Military Experience of John Hunter on Himself and the Military Surgeon of Today. *Lancet*, Lond. 1:249-254, 1917.

308. MALAN, E. Treatment of Chronic Obliterative Arterial Disease With Venous Autografts. *Boll. Soc. piemont. Chir.* 22:705, 1952.
309. MARRANGONI, A. C., and CECCHINI, L. P. Homotransplantation of Arterial Segments Preserved by the Freeze-Drying Method. *Ann. Surg.* 134:977-983, 1951.
310. MARTINEZ, N. S., DAHL, E. V., and GRINDLAY, J. H. Early Tissue Response to Polyvinyl Sponge Aortic Grafts. *Surgery* 42:1002-1013, 1957.
311. MASON, E. C. A Note on the Use of Heparin in Blood Transfusion. *J. Laborat. Clin. M.* 10:203-206, 1924.
312. MATAS, R. An Operation for the Radical Cure of Aneurysm Based Upon Arteriorrhaphy. *Ann. Surg.* 37:161-196, 1903.
313. ———. Some Experiences and Observations in the Treatment of Arteriovenous Aneurysms by the Intrasaccular Method of Suture (Endo-Aneurismorrhaphy) with Special Reference to the Transvenous Route. *Ann. Surg.* 71:403-427, 1920.
314. ———. Cited in *Ann. Surg.* 71:403-427, 1920.
315. ———. Response to Forward. *Surgery* 34:972-984, 1953.
316. MATHESON, N. M., and MURRAY, G. Recent Advances and Experimental Work in Conservative Vascular Surgery. (In *Surgery of Modern Warfare*—Edited by Hamilton Bailey). The Williams and Wilkins Co., Baltimore, 1941, 1:324-327.
317. MAURER, A. Wounds of the Vessels of the Face, Neck, and Limbs. Their Surgical Treatment, Based upon Four Hundred and Forty-Three Cases. *Internat. Clin.* 31:164-195, 1921.
318. ———. Note sur les Plaies Vasculaires Récentes et leur Traitement, d'Après 444 Observations. *Mem. Acad. de chir.* 65:1156-1164, 1939.
319. MAZZEO, F., and INFRANZI, A. Note Istologiche Sulla Conservazione Sperimentale di Arterie in Soluzioni al Cortisone. *Ann. ital. chir.* 31:43-54, 1954.
320. MCAFEE, J. G. A Survey of Complications of Abdominal Aortography. *Radiology* 68:825-838, 1957.
321. MCALLISTER, F. F., LEICHNINGER, D., and BECK, C. Revascularization of the Heart by Vein Graft from Aorta to Coronary Sinus. *Ann. Surg.* 133:153-165, 1951.
322. MCBURNEY, R. P., and LOVELACE, J. R. Acute Rupture of Abdominal Aortic Aneurysm with Resection, Graft and Recovery. *J. Tennessee M. Ass.* 50:458-464, 1957.
323. MCCAUGHAN, J. J. The Experimental Use of Ivalon Arterial Grafts. *Surgery* 42:717-721, 1957.
324. MCCUNE, W. S., THISTLETHWAITE, J. R. KESHISHIAN, J. M., and BLADES, B. The Nutrition of Blood Vessel Grafts: An India Ink Injection Study of their Vascularization. *Surg. Gyn. Obst.* 94:311-316, 1952.
325. MCKENZIE, A. D., and ROBERTSON, H. R. Arterial Reconstruction (Thromboendarterectomy) in Arteriosclerotic Vascular Disease—A Report of Two Successful Cases. *Surgery* 36:808-813, 1954.
326. MCKENZIE, A. D., SUTHERLAND, W. H., COLBECK, J. C., MOYES, P., and SANDY, T. Arterial Preservation and Grafting. *Canad. M. Ass. J.* 71:389-391, 1954.
327. MCKHANN, C. F., BELNAP, W. D., and BECK, C. S. Cervical Arteriovenous Anastomosis in Treatment of Mental Retardation, Convulsive Disorders and Cerebral Spasticity. *Ann. Surg.* 132:162-175, 1950.
328. MCLEAN, J. The Thromboplastic Action of Cephalin. *Am. J. Physiol.* 41:250-257, 1916.

329. MacKenzie, R. J., Buell, A. H., and Pearson, S. C. Aneurysm of Aortic Homograft with Rupture into the Duodenum. *A.M.A. Arch. Surg.* 77:965-969, 1958.

330. Meeker, I. A., Jr., and Gross, R. E. Sterilization of Frozen Arterial Grafts by High-Voltage Cathode-Ray Irradiation. *Surgery* 30:19-28, 1951.

331. Melick, W. F., and Vitt, A. E. Present Status of Aortography. *J. Urol., Balt.* 60:321-334, 1948.

332. Merendino, K. A., Girvin, G. W., and Thomas, G. I. The Clinical Use of Teflon Tubes as a Vascular Substitute for Major Arteries. *Surgery* 43:959-968, 1958.

333. Meyer, W. Final Results of Arteriovenous Anastomosis (Femoral) for Gangrene of Foot. *Ann. Surg.* 62:630, 1915.

334. Miller, H. H., Callow, A. D., Welch, C. S., and MacMahon, H. E. The Fate of Arterial Grafts in Small Arteries: An Experimental Study. *Surg. Gyn. Obst.* 92:581-588, 1951.

335. Mitchiner, P. H. Injuries of Blood Vessels and Their Treatment. *St. Thomas' Hosp. Gaz.* 38:92-96, 1940.

336. Moeys, E. J., Mreyen, F. W., and den Hartog, B. J. C. Homotransplantation of Formaldehyde-Preserved Arteries in Dogs: A Fundamental Study. *Arch. chir. neerl.*, (supp.) 6:333-440, 1954.

337. Moniz, E. L'Encéphalographie Artérielle, son Importance dans la Localisation des Tumeurs Cérébrales. *Rev. neurol.* 2:72-90, 1927.

338. Montgomery, M. L. Effect of Therapeutic Venous Ligation on Blood Flow in Cases of Arterial Occlusion. *Proc. Soc. Exp. Biol., N. Y.* 27:178-179, 1929.

339. Moore, C. H., and Murchison, C. *On a New Method of Procuring the Consolidation of Fibrin in Certain Incurable Aneurysms.* London, 1864, pp. 21.

340. Moore, H. D. The Replacement of Blood Vessels by Polythene Tubes. *Surg. Gyn. Obst.* 91:593-600, 1950.

341. Moore, T. C. Discussion of paper by Schauble, J. F., Anlyan, W. G., Postlethwait, R. W., "A Study of Grafts in the Venous System." *A.M.A. Arch. Surg.* 78:288-292, 1959.

342. Moore, T. C., Riberi, A., and Kajikuri, H. Freeze-Dried and Alcohol Preserved Homografts for Replacement of Small Arteries. *Surg. Gyn. Obst.* 103:155-162, 1956.

343. Moretz, W. H. Discussion of paper by Deterling, R. A., Jr., and Bhonslay, S. G., "An Evaluation of Synthetic Materials and Fabrics Suitable for Blood Vessel Replacement." *Surgery* 38:71-91, 1955.

344. Mortensen, J. D., Edwards, J. E., Grindlay, J. H., and Kirklin, J. W. Reinforcement of Fresh Autogenous Venografts to Aorta: Experimental Study with Polyvinyl Formalinized (Ivalon) Sponge. *A.M.A. Arch. Surg.* 70:545-554, 1955.

345. Mortensen, J. D., and Grindlay, J. H. Molded, Seamless Tubes of Polyvinyl Formalinized Sponge. *A.M.A. Arch. Surg.* 72:871-878, 1956.

346. Mortensen, J. D., Weed, L. A., and Grindlay, J. H. Maintaining Sterility During Storage of Arterial Homografts. *J. Laborat. Clin. M.* 44:604-608, 1954.

347. Morton, J. H., and Mahoney, E. B. The Use of Heterogenous Vein and Artery Grafts Supported by a Plastic Sponge. *Surg. Forum* 5:229-235, 1954.

348. Muller, W. H., Jr., Liddle, H. V., and Edmunds, M. C., Jr. Surgical Management of Arterial Obliterative Disease: Special Reference to Thromboendarterectomy. *Ann. Surg.* 147:845-853, 1958.

349. MULVIHILL, D. A., HARVEY, S. C., and DOROSZKA, V. Simultaneous Ligation of Vein in Ligation of Large Arteries: Experimental Study. *Am. J. Surg.* 13:431-452, 1931.
350. MUNRO, J. C. Ligation of the Ductus Arteriosus. *Ann. Surg.* 46:335-338, 1907.
351. MURRAY, G. Heparin in Surgical Treatment of Blood Vessels. *A.M.A. Arch. Surg.* 40:307-325, 1940.
352. MURRAY, G. D. W. Heparin in Thrombosis and Embolism. *Brit. J. Surg.* 27:567-598, 1940.
353. MURRAY, G. Heparin in Thrombosis and Blood Vessel Surgery. *Surg. Gyn. Obst.* 72:340-344, 1941.
354. MURRAY, G. Symposium on Vascular Problems: Surgical Repair or Injuries to Main Arteries. *Am. J. Surg.* 83:480-483, 1952.
355. MURRAY, G. D. W., and BEST, C. H. The Use of Heparin in Thrombosis. *Ann. Surg.* 180:163-177, 1938.
356. MURRAY, G., and JANES, J. M. Prevention of Acute Failure of Circulation Following Injuries to Large Arteries; Experiments with Glass Cannulae Kept Patent by Administration of Heparin. *Brit. M. J.* 2:6-7, 1940.
357. NABATOFF, R. A., TOUROFF, A. S. W., and GROSS, M. Four Year Studies Concerning the Fate of Experimental Vena Cava Autografts Used to Bridge Aortic Defects. *Surg. Gyn. Obst.* 101:20-24, 1955.
358. NAGEOTTE, J., and SENCERT, L. Greffes Fonctionnelles d'Artéres Mortes. *C. rend. Acad. d. Sc.*, Par. 167:793-796, 1918.
359. NEFF, J. M. Blood Vessel Suture. *Surg. Gyn. Obst.* 33:657-669, 1921.
360. NELSON, O. A. Arteriography of Abdominal Organs by Aortic Injection. *Surg. Gyn. Obst.* 74:655-662, 1942.
361. NEWTON, W. T., WEICHSELBAUM, T. E., and BUTCHER, H. R., JR. Equine Arterial Heterografts Altered by Controlled Enzymatic Digestion. *A.M.A. Arch. Surg.* 73:432-439, 1956.
362. NYHUS, L. M., and HARKINS, H. N. The Present Status of Vascular Grafts. *West. J. Surg.* 62:166-172, 1954.
363. ———. Autogenous Vein Grafts. *Surgery* 42:762-766, 1957.
364. NYHUS, L. M., KANAR, E. A., MOORE, H. G., JR., SCHMITZ, E. J., SAUVAGE, L. R., and HARKINS, H. N. Experimental Vascular Grafts: III. The Dimensional Changes in Short and Long Length Fresh and Preserved Aortic Homografts Implanted into the Thoracic Aorta of Growing Pigs: A Preliminary Report. *Surg. Gyn. Obst.* 97:81-86, 1953.
365. NYHUS, L. M., KANAR, E. A., MOORE, H. G., JR., SCHMITZ, E. J., ZECH, R. K., SAUVAGE, L. R., and HARKINS, H. N. Experimental Vascular Grafts: IV. Arterial Homograft Degeneration. *Am. Surgeon* 21:289-307, 1955.
366. NYHUS, L. M., MOORE, H. G., JR., ZECH, R. K., KANAR, E. A., GRIFFITH, C. A., EADE, G. G., and HARKINS, H. N. Experimental Vascular Grafts: VI. A Viable Muscle Support for Venous Autografts Implanted into the Thoracic Aorta. *West. J. Surg.* 64:497-503, 1956.
367. OECONOMOS, N., and HEWITT, J. Résultáts des Greffes Vasculaires; Étude Expérimentale et Clinique â Propos des Homo et Hétérogreffes. *Sem. hop., Paris* 28:1538-1547, 1952.
368. OUDOT, J. Cited by Gross, R. E., Bill, A. H., Jr., and Peirce, E. C., II. "Methods for Preservation and Transplantation of Arterial Grafts: Observations on Arterial Grafts in Dogs; Report of Transplantation of Preserved Arterial Grafts in Nine Human Cases." *Surg. Gyn. Obst.* 88:689-701, 1949.

369. ———. Un Deuxième cas de Greffe de la Bifurcation Aortique pour Thrombose de la Fourche Aortique. *Mém. Acad. chir.*, Par. 77:644-645, 1951.

370. ———. La Greffe Vasculaire dans les Thromboses du Carrefour Aortique. *Presse méd.* 59:234-236, 1951.

371. ———. Un Nouveau cas de Greffe de Bifurcation Aortique. *Mém. Acad. chir.*, Par. 77:1035-1036, 1951.

372. Oudot, J., and Beaconsfield, P. Thrombosis of Aortic Bifurcation Treated by Resection and Homograft Replacement: Report of Five Cases. *A.M.A. Arch. Surg.* 66:365-374, 1953.

373. Ouzounian, G. S. Arterial Grafting with Yard-Goods Nylon Cloth. *A.M.A. Arch. Surg.* 73:192-196, 1956.

374. Owen, K. Polyvinyl Alcohol Sponge as an Arterial Substitute. *Proc. R. Soc. M.*, Lond. 49:340-342, 1956.

375. Paolucci, R., and Tosatti, E. Homografts of Aorta Preserved in Alcohol. *J. Internat. Coll. Surgeons* 14:257-261, 1950.

376. Pate, J. W., Sawyer, P. N., Detterling, R. A., Jr., Blunt, J. W., and Parshley, M. S. Early Results in the Experimental Use of Freeze-Dried Arterial Grafts. *Surg. Forum* 3:147-151, 1952.

377. Payne, J. H., Rudy, N. E., and Winsor, T. The By-Pass Graft, Its Use in Arterial Occlusive Disease. *Am. J. Surg.* 94:171-181, 1957.

378. Payr, E. Beiträge zur Technik der Blutgefäss-und Nervennaht Mebst Mittheilungen über die Verwendung Eines Resorbirbaren Metalles in der Chirurgie. *Arch. f. Klin. Chir.* 62:67-93, 1900.

379. Peirce, E. C., II. Preservation of Endothelium in Refrigerated Aortic Segments and in Aortic Homografts in Dogs as Shown by Silver Staining. *Anat. Rec.* 112:831-838, 1952.

380. Peirce, E. C., II., Gross, R. E., Bill, A. H., Jr., and Merrill, K., Jr. Tissue-Culture Evaluation of the Viability of Blood Vessels Stored by Refrigeration. *Ann. Surg.* 129:333-348, 1949.

381. Peirce, E. C., II., Rheinlander, H. F., Moritz, A. R., Gross, R. E., and Merrill, K., Jr. Transplantation of Aortic Segments Fixed in 4 Per Cent Neutral Formalin. *Am. J. Surg.* 78:314-323, 1949.

382. Phelan, J. T., Botham, R. J., Young, W. P., and Schmidt, E. R. The Effect of Suture Material in Determining the Patency of Small Artery Grafts. *Surgery* 43:969-973, 1958.

383. Poole, J. C. F., Sanders, A. G., and Florey, H. W. The Regeneration of Aortic Endothelium. *J. Path. Bact.*, Lond. 75:133-143, 1958.

384. Poppe, J. K., and de Oliviera, H. R. Treatment of Syphilitic Aneurysms by Cellophane Wrapping. *J. Thorac. Surg.* 15:186-195, 1946.

385. Poth, E. J., Johnson, J. K., and Childers, J. H. The Use of Plastic Fabrics as Arterial Prostheses. *Ann. Surg.* 142:624-632, 1955.

386. Pratt, G. H. The Surgical Problem in Replacement Aortic and Arterial Grafts. *Surg. Gyn. Obst.* 107:107-112, 1958.

387. Propping, K. Über die Ursache der Gangrän nach Unterbindung Grosser Arterien. *Munch. med. Wschr.* 64:598-599, 1917.

388. Radlinski. Quoted by Antonucci, C., "Un Nuovo Schema di Anastomosi Arterio-Venosa Nella Cura Delle Gangrene Degli Arti Inferiori da Endoangioite Obliterante." *Arch. ed atti Soc. ital. di chir.* 36:756-762, 1930.

389. Reboul, H., and Huguier, J. Endartériectomie Aortico-Iliaque Gauche Datant de Seize Mois. *Mém. Acad. chir.*, Par. 75:318, 1949.

390. REBOUL, H., and LAUBRY, P. Endarteriectomy in the Treatment of Chronic Endarteritis Obliterans of the Limb and Abdominal Aorta. *Proc. R. Soc. M.*, Lond. 43:547-552, 1950.

391. REID, M. R. The Effect of Arteriovenous Fistula Upon the Heart and Blood Vessels. An Experimental and Clinical Study. *Bull. Johns Hopk. Hosp.* 31:43-50, 1920.

392. RENAUX, L. Reconstruction of Popliteal Artery. *Brazil-med.* 34:509, 1920.

393. ROB, C. G. Preservation and Transplantation of Human Tissues. *Lancet*, Lond. 267:255-258, 1954.

394. ———. The Preservation of Arterial Grafts by Freeze Drying. *Proc. R. Soc. M.*, Lond. 47:368-370, 1954.

395. ———. The Surgery of the Abdominal Aorta and Its Major Branches. *Ann. R. Coll. Surgeons*, England. 17:307-317, 1955.

396. ROB, C. G., and EASTCOTT, H. H. G. *Arterial Grafting.* Brit. Surg. Progress, London, Butterworth and Co., Ltd., 1953.

397. ROBB, G. P., and STEINBERG, I. The Practical Method of Visualization of the Chambers of the Heart, the Pulmonary Circulation and the Great Blood Vessels in Man. *J. Clin. Invest.* 17:507, 1938.

398. ROSENBERG, N., GAUGHRAN, E. R. L., HENDERSON, J., LORD, G. H., and DOUGLAS, J. F. The Use of Segmental Arterial Implants Prepared by Enzymatic Modification of Heterologous Blood Vessels. *Surg. Forum* 6:242-246, 1955.

399. ROSENBERG, N., HENDERSON, J., DOUGLAS, J. F., LORD, G. H., and GAUGHRAN, E. R. L. The Use of Arterial Implants Prepared by Enzymatic Modification of Arterial Heterografts; II. The Physical Properties of the Elastica and Collagen Components of the Arterial Wall. *A.M.A. Arch. Surg.* 74:89-95, 1957.

400. ROSENBERG, N., HENDERSON, J., LORD, G. H., GAUGHRAN, E. R. L., and DOUGLAS, J. F. Use of Enzyme-Digested Heterografts as Segmental Arterial Substitutes. III. Follow-up Observations on Two-Year-Old Aortic Implants. *A.M.A. Arch. Surg.* 76:275-281, 1958.

401. ROSS, D. N. Formalin Sterilization of Arterial Homografts. *Guy's Hosp. Rep.*, Lond. 103:71-79, 1954.

402. ROSS, R. L. Thromboendarterectomy in Occlusive Arterial Disease: Pathologic Examination a Year and a Half After Operation. *California M.* 87:332-335, 1957.

403. ROUSSELOT, L. M. Autogenous Vein Grafts in Splenorenal Anastomosis: A Description of Technique and its Clinical Application in Seven Patients. *Surgery* 31:403-410, 1952.

404. RÜHL, R. Über Konservierung von Arterientransplantaten. *Arch. klin. Chir.* 267:197-198, 1951.

405. RUSTAD, H. I., GREGG, R. O., and PRIOR, J. T. The Effect of Hypercholesterolemia Upon Aortic Homografts and Teflon-Nylon Prostheses in the Rabbit. *Surgery* 44:726-734, 1958.

406. SAKO, Y. Prevention of Dilatation in Autogenous Venous and Pericardial Grafts in the Thoracic Aorta: An Experimental Study. *Surgery* 30:148-160, 1951.

407. SAKO, Y., CHISHOLM, T. C., MERENDINO, K. A., and VARCO, R. L. An Experimental Evaluation of Certain Methods of Suturing the Thoracic Aorta. *Ann. Surg.* 130:363-383, 1949.

408. SANDBLOM, P. The Effect of Injury on Wound Healing. *Ann. Surg.* 129:305-314, 1949.

409. SAUTOT, J., BOST, J., and TOURAINE, Y. Greffes Artérielles Hétérogènes. *Presse méd.* 60:244-246, 1952.

410. SAUVAGE, L. R., and HARKINS, H. N. An Experimental Study of the Effects of Preservation on the Fate of Aortic and Vena-Caval Homografts in the Growing Pig. *Ann. Surg.* 136:439-458, 1952.

411. ——. Growth of Vascular Anastomoses: An Experimental Study of the Influence of Suture Type and Suture Method With a Note on Certain Mechanical Factors Involved. *Bull. Johns Hopk. Hosp.* 91:276-297, 1952.

412. ——. Experimental Vascular Grafts: An Evaluation Relating to Types, Means of Preservation, and Methods of Suture in the Growing Pig. *Surgery* 33:587-635, 1953.

413. ——. Some Observations of the Growth Characteristics of Various Types of Vascular Grafts: An Experimental Study in the Growing Pig. *West. J. Surg.* 62:7-11, 1954.

414. SAUVAGE, L. R., and WESOLOWSKI, S. A. The Healing and Fate of Arterial Grafts. *Surgery* 38:1090-1131, 1955.

415. SAUVAGE, L. R., WESOLOWSKI, S. A., and PINC, R. D. Freeze-Dry Process for Arteries. *Surgery* 37:585-601, 1955.

416. SCHAUBLE, J. F., ANLYAN, W. G., and POSTLETHWAIT, R. W. A Study of Grafts in the Venous System. *A.M.A. Arch. Surg.* 78:288-292, 1959.

417. SCHENK, W. G., JR., COSGRIFF, J. H., and GRAY, J. G. Hemodynamic Changes Resulting from Blood Vessel Grafts and Postheses. *Surg. Gyn. Obst.* 103:212-220, 1956.

418. SCHIMERT, G., HADIDIAN, C. Y., and BRANTIGAN, O. C. Temporary Bypass for Repair of Aneurysms of the Aortic Arch. *J. Am. M. Ass.* 164:1089-1091, 1957.

419. SCHLOSS, G., and SHUMACKER, H. B., JR. Studies in Vascular Repair. IV. The Use of Free Vascular Transplants for Bridging Arterial Defects. An Historical Review with Particular Reference to Histological Observations. *Yale J. Biol.* 22:273-290, 1949.

420. SCHMITZ, E. J., KANAR, E. A., SAUVAGE, L. R., STORER, E. H., and HARKINS, H. N. The Influence of Diameter Disproportion and of Length on the Incidence of Complications in Autogenous Venous Grafts in the Abdominal Aorta. *Surgery* 33:190-206, 1953.

421. SCOTT, V. Abdominal Aneurysms; Report of 96 Cases. *Am. J. Syph.* 28:682-710, 1944.

422. SEHRT, E. Über Die Künstliche Blutleere von Gliedmassen and Unterer Körperhälfte, Sowie Über die Ursache der Grangrän des Gliedes nach Unterbindung der Arterien Allein. *Med. Klin.*, Berl. 12:1338-1341, 1916.

423. SEIDENBERG, B., HURWITT, E. S., and CARTON, C. A. The Technique of Anastomosing Small Arteries. *Surg. Gyn. Obst.* 106:743-746, 1958.

424. SELF, M. M., COOLEY, D. A., DEBAKEY, M. E., and CREECH, O., JR. The Use of Braided Nylon Tubes for Aortic Replacement. *Ann Surg.* 142:836-843, 1955.

425. SENCERT, L. La Chirurgié des gros Vaisseaux: I. Les Blessures des Vaisseaux. Cinquiemè Congrès de la Société Internationale de Chirurgié, Paris. 19-23, Juillet 1920.

426. SEWELL, W. H., BATCHELOR, W. H., and KOTH, D. R. The Importance of Elastic Lamellae in Aortic Grafts, and a Technique for the Experimental Production of Aortic Aneurysms. *Surg. Forum* 5:264-268, 1954.

427. SHAW, R. S., and WHEELOCK, F. Blood Vessel Grafts in the Treatment of Chronic Occlusive Disease in the Femoral Artery. *Surgery* 37:94-104, 1955.

428. Shumacker, H. B., Jr. The Problems of Maintaining the Continuity of the Artery in the Surgery of Aneurysms and Arteriovenous Fistulae. *Ann. Surg.* 127:207-230, 1948.

429. ———. Plastic Grafts for Aortic Substitution in Man. *A.M.A. Arch. Surg.* 75:413-422, 1957.

430. Shumacker, H. B., Jr., Freeman, L. W., Hutchings, L. M., and Radigan, L. Studies in Vascular Repair. VI. Further Observations on the Growth of Anastomoses and Free Vascular Transplants in Growing Animals. *Angiology* 2:263-269, 1951.

431. Shumacker, H. B., Jr., Harris, E. J., and Siderys, H. Pliable Plastic Tubes as Aortic Substitutes. *Surgery* 37:80-93, 1955.

432. Shumacker, H. B., Jr., Kajikuri, H., Grice, P., Rodriguez, R., Riberi, A. Moore, T. C., and Siderys, H. Comparative Experimental Study of Aortic Grafts. *Surgery* 41:943-957, 1957.

433. Shumacker, H. B., Jr., and King, H. The Use of Pliable Plastic Tubes as Aortic Substitutes in Man. *Surg. Gyn. Obst.* 99:287-294, 1954.

434. ———. Surgical Treatment of Ruptured Aortic Aneurysms. *A.M.A. Arch. Surg.* 71:768-774, 1955.

435. Shumacker, H. B., Jr., Schloss, G., Freeman, L. W., Wayson, E. E., and Stahl, N. H. Studies in Vascular Repair. V. Experiments with the Use of Free Venous Transplants for Bridging Aortal Defects. *Yale J. Biol.* 23:81-93, 1950.

436. Shumway, N. E., Gliedman, M. L., and Lewis, F. J. An Experimental Study of the Use of Polyvinyl Sponge for Aortic Grafts. *Surg. Gyn. Obst.* 100:703-706, 1955.

437. Shumway, N. E., Lewis, F. J., and Gliedman, M. L. Plastic Blood Vessels made of Polyvinyl Sponge. *Lancet*, Lond. 75:348-350, 1955.

438. Sicard, J. A., and Forestier, G. Injections Intra-Vasculaires d'Huile Iodée sous Contrôle Radiologique. *C. rend. Soc. biol.* 88:1200-1202, 1923.

439. Simeone, F. A., Grillo, H. C., and Rundle, F. On the Question of Ligation of the Concomitant Vein when a Major Artery is Interrupted. *Surgery* 29:932-951, 1951.

440. Smith, P. G., Rush, T. W., and Evans, A. T. The Technique of Translumbar Arteriography. *J. Am. M. Ass.* 148:255-258, 1952.

441. Southgate, W. A., Fomon, J. J., and Mahoney, E. B. Fate of Splinted Venous Homo- and Autografts in Thoracic Aorta of Dogs. *Angiology* 6:427-441, 1955.

442. Stetten, D. The Futility of Arteriovenous Anastomosis in the Treatment of Impending Gangrene of the Lower Extremity. *Surg. Gyn. Obst.* 20:381-402, 1915.

443. Stich, R., and Zoeppritz, H. Zus Histologie der Gefassnaht, der Gefass und Organ Transplantationen. *Beitr. path. Anat.* 46:337, 1909.

444. Sutherland, T. W., Williamson, G. M., Zinnemann, K., and Shucksmith, H. S. Graft Sterilization: A Bacteriological and Histological Study of the Merits of Ethylene Oxide and B-Propiolactone as Tissue Sterilizing Agents, with Special Reference to Arterial Grafts. *Brit. M. J.* 1:734-736, 1958.

445. Swan, H., Robertson, H. T., and Johnson, M. E. Arterial Homografts. I. The Fate of Preserved Aortic Grafts in the Dog. *Surg. Gyn. Obst.* 90:568-579, 1950.

446. Swann, W. K., and Bradsher, J. T., Jr. Acute Dissecting Aneurysm of the Aorta: Operation, with Recovery. *N. England J. M.* 255:36-37, 1956.

447. Swenson, O., and Gross, R. E. Absorbable Fibrin Tubes for Vein Anastomoses. *Surgery* 22:137-143, 1947.

448. SZILAGYI, D. E., FRANCE, L. C., SMITH, R. F., and WHITCOMB, J. G. The Clinical Use of an Elastic Dacron Prosthesis. *A.M.A. Arch. Surg.* 77:538-551, 1958.

449. SZILAGYI, D. E., JAY, G. D., III, and MUNNELL, E. D. Femoral Arteriovenous Anastomosis in the Treatment of Occlusive Arterial Disease. *A.M.A. Arch. Surg.* 63:435-451, 1951.

450. SZILAGYI, D. E., MCDONALD, R. T., SMITH, R. F., and WHITCOMB, J. G. Biologic Fate of Human Arterial Homografts. *A.M.A. Arch. Surg.* 75:506-529, 1957.

451. SZILAGYI, D. E., and OVERHULSE, P. R. Segmental Aorto-Iliac and Femoral Arterial Occlusion. Treatment by Resection and Arterial Graft Replacement. *J. Am. M. Ass.* 157:426-433, 1955.

452. SZILAGYI, D. E., OVERHULSE, P. R., SHONNARD, C. P., and LOGRIPPO, G. A. The Sterilization of Human Arterial Homografts with Beta-Propiolactone. *Surg. Forum* 5:244-252, 1954.

453. SZILAGYI, D. E., SHONNARD, C. P., LOPEZ, J. L., and SMYTH, N. P. D. The Replacement of Long and Narrow Arterial Segments: An Experimental Study of Heterografts and Seamless Woven Nylon and Teflon Prostheses. *Surgery* 40:1043-1059, 1956.

454. SZILAGYI, D. E., SMITH, R. F., and OVERHULSE, P. R. Resectional Surgery of the Abdominal Aorta: Problems of Case Selection and Operative Technique. *A.M.A. Arch. Surg.* 71:491, 1955.

455. SZILAGYI, D. E., WHITCOMB, J. G., and SHONNARD, C. P. Replacement of Long and Narrow Arterial Segments. II. Experimental Studies With an Elastic ("Helanca") Seamless Woven Nylon Prosthesis. *A.M.A. Arch. Surg.* 74:944-953, 1957.

456. SZILAGYI, D. E., WHITCOMB, J. G., and SMITH, R. F. The Causes of Late Failures in Grafting Therapy of Peripheral Occlusive Arterial Disease. *Ann. Surg.* 144:611-634, 1956.

457. TIBBS, D. J. Personal communication to the authors, 1958.

458. TIBBS, D. J., and LESLIE, W. G. Arterial Replacement with Minimal Interruption of Blood-Flow. *Lancet*, Lond. 1:292-294, 1958.

459. TRAFAS, P. C., CARLSON, R. E., LOGRIPPO, G. A., and LAM, C. R. Chemical Sterlization of Arterial Homografts. *A.M.A. Arch. Surg.* 69:415-424, 1954.

460. TUFFIER, T. De l'Intubation dans les Plaies des Grosses Arteres. *Bull. Acad. nat. méd.*, Par. 74:455-460, 1915.

461. TUFFIER, T. Anévrisme Artério-Veineux du Canal de Hunter. Résection des Vaisseaux. Anastomose des deux Bouts de l'Artere Réséquée, par un Tube d'Argent Paraffine (Intubation Artérielle), Permettant à la Circulation Artérielle de Sèffectuer. *Bull. Soc. chir.*, Par. 43:739-742, 1917.

462. TUFFIER, T. Le Traitement Chirurgical des Anévrismes de l'Aorte. *Bull. Acad. méd.*, Par. 85:586-589, 1921.

463. TUNE, L. J., and OWENS, J. C. The Development of Experimental Aneurysms in Lyophilized Arterial Heterografts. *Surg. Forum* 5:258-264, 1954.

464. VARGAS, L. R., and DETERLING, R. A., JR. The Use of Nylon Net for the External Support of Blood Vessel Grafts and Aneurysms. *Surgery* 34:1061-1075, 1953.

465. VISALLI, F. Note Istologiche Sulla Conservazione Sperimentale di Arterie in Glicerina. *Policlinico (sez. chir.)* 57:233-237, 1950.

466. VISALLI, F., and NATELLIS, F. Tentativi Operatori Sperimentali di Omoinnesti di Arterie Conservate in Glicerina. *Policlinico (sez. chir.)* 57:297.304, 1950.

467. Vogelfanger, I. J., and Beattie, W. G. A Concept of Automotion in Vascular Surgery: A Preliminary Report on a Mechanical Instrument for Arterial Anastomosis. *Canad. J. Surg.* 1:262-265, 1958.
468. Von Bonin, G. Aneurysmen Durch Schussverletzung und ihre Behandlung. *Beitr. z. klin. Chir.* 97:146-176, 1915.
469. Voorhees, A. B., Jr., Jaretzki, A., III, and Blakemore, A. H. The Use of Tubes Constructed from Vinyon "N" Cloth in Bridging Arterial Defects. *Ann. Surg.* 135:332-336, 1952.
470. Wagner, F. B., Jr., Price, A. H., and Swenson, P. C. Abdominal Arteriography: Technique and Diagnostic Application. *Am. J. Roentg.* 58:591-598, 1947.
471. Warren, R. Discussion of paper by Szilagyi, D. E., Whitcomb, J. G. and Smith, R. F. *Ann. Surg.* 144:632, 1956.
472. Warren, R. Evaluation of Thromboendarterectomy for Arteriosclerosis Obliterans of the Femoral Artery. *Surg. Gyn. Obst.* 104:571-578, 1957.
473. Warren, W. D., Beckwith, J., and Muller, W. H., Jr. Problems in the Surgical Management of Acute Dissecting Aneurysm of the Aorta. *Ann. Surg.* 144:530-548, 1956.
474. Wehn, P. S. Incisions and Sutures in Arteries. *Acta chir. scand.* 108:231-238, 1954.
475. Weis, J. Ergebnisce bei 20 Hundeversuchen mit Gefasstransplantationen an der Aorta. *Arch. klin. Chir.* 267:569-575, 1951.
476. Weiss, E. W., and Lam, C. R. Tantalum Tubes in the Non-Suture Method of Blood Vessel Anastomosis. *Am. J. Surg.* 80:452-454, 1950.
477. Welch, J. S., Kirklin, J. W., Ellis, F. H., Jr., and Bruwer, A. J. Resection and Grafting for Chronic Occlusion of the Terminal Aorta or Iliac Arteries. *J. Am. M. Ass.* 164:1045-1049, 1957.
478. Wesolowski, S. A., and Sauvage, L. R. Comparison of the Fates of Orlon Mesh Prosthetic Replacement of the Thoracic Aorta and Aorta Bifurcation. *Ann. Surg.* 143:65-72, 1956.
479. ———. Heterologous Aortic Grafts—with Special Reference to Recipient Site, Ethylene Oxide Freeze-Dry Preparation and Species of Origin. *Ann. Surg.* 145:187-198, 1957.
480. Wheelock, F., and Shaw, R. S. Aneurysm of the Abdominal Aorta and Iliac Arteries. *N. England J. M.* 255:72-76, 1956.
481. Whitcher, J. R., and Movius, H. Thromboendarterectomy in Segmental Arterial Occlusion. *West. J. Surg.* 63:671-676, 1955.
482. Whittlesdy, R. H., Sekerak, N. M., Blunt, J. W., Jr., and Hudack, S. S. Observations of Elastic Synthetic Fabric Sleeves as Vascular Protheses. *A.M.A. Arch. Surg.* 73:440-454, 1956.
483. Wilson, W. C. Occlusion of the Main Artery and Main Vein of a Limb. *Brit. J. Surg.* 20:393-411, 1933.
484. Wright, I. S., Urdaneta, E., and Wright, B. Re-Opening the Case of the Abdominal Aortic Aneurysm. *Circulation*, N. Y. 13:754-768, 1956.
485. Wylie, E. J., Gardner, R. E., Johansen, R., and McCorkle, H. J. An Experimental Study of Regional Heparinization. *Surgery* 28:29-36, 1950.
486. Wylie, E. J. Thromboendarterectomy for Arteriosclerotic Thrombosis of Major Arteries. *Surgery* 32:275-292, 1952.
487. ———. Discussion of paper by Freeman, N. E., and Nicholson, G. J. *A.M.A. Arch. Surg.* 78:286, 1959.
488. Wylie, E. J., and Gardener, R. Thromboendarterectomy, a Clinical Appraisal. *Surgery* 37:415-426, 1955.

489. Wylie, E. J., Kerr, E., and Davies, O. Experimental and Clinical Experiences with the Use of Fascia Lata Applied as a Graft About Major Arteries After Thromboendarterectomy and Aneurysmorrhaphy. *Surg. Gyn. Obst.* 93:257-272, 1951.

490. Wylie, E. J., and McGuinness, J. S. The Recognition and Treatment of Arteriosclerotic Stenosis of Major Arteries. *Surg. Gyn. Obs.* 97:425-433, 1953.

491. Yamanouchi, H. Über die Zirkulären Gefässnähte und Arterienvenen-Anastomosen, Sowie Über die Gefässtransplantationen. *Deut. Zschr. Chir.* 112:1-118, 1911.

492. Zech, R. K., Nyhus, L. M., Kanar, E. A., Schmitz, E. J., Sauvage, L. R., Moore, H. G., Jr., Fletcher, T. L., Merendino, K. A., and Harkins, H. N. Experimental Vascular Grafts. VII. The Effects of Dicetyl Phosphate on Venous Autografts Implanted in the Thoracic Aorta of Growing Pigs. *Angiology* 5:439-448, 1954.

493. Ziperman, H. H. Acute Arterial Injuries in the Korean War—A Statistical Study. *Ann. Surg.* 139:1-8, 1954.

BIOGRAPHICAL NOTE

Dr. Charles Claude Guthrie was born on May 13, 1880 near Wentzville, St. Charles County, Missouri, the son of Robert McCluer Guthrie (1833-1914) and Fannie Hall Guthrie (1845-1923). The family had come to Pennsylvania from Scotland in 1700, and had moved successively into South Carolina, Kentucky, Tennessee and finally Missouri. In 1816 Dr. Guthrie's grandfather, Robert Guthrie, bought and settled upon a Spanish Land Grant in St. Charles County. Here he spent his life, reared his family, and subsequently died in 1847.

Dr. Guthrie's father, Robert, joined two brothers in California and spent four years gold mining. How successful this adventure was is not known, but Robert did return to the family farm in Missouri and was able to buy out the other heirs. In 1871, he married Fannie Hall of Virginia and eventually had five children by her. In 1899 the family moved to Columbia, Missouri, where the younger children were educated.

Since he was brought up on a farm, it was natural that Charles Claude Guthrie's youthful interests should have included hunting, fishing, and nature study. He actually made his own first gun, and developed into an excellent "wingshot." His observations of insects resulted in "a few notes" being published in *Science*. His interest in agricultural problems was life-long, and he later published studies on the preservation of meat and fowl by rapid pickling, and of many other food stuffs by rapid drying through absorption. Indian and pre-Indian artifacts apparently abounded on his family's farm, and among other identifiable stone relics he once found a stone counterweight for an ancient throwing stick (Atlatl). It is remarkable that he guessed correctly that these objects were of pre-Indian origin. The counterweight was recently examined at the American Museum of Natural History by Dr. James A. Ford who believes it to have been made by a pre-Indian race which lived in the area about 2,000 years ago.

Dr. Guthrie received the B.S. from Woodlawn Institute in O'Fallon, Missouri and the M.D., in 1901, from Missouri State University (now the University of Missouri). His scientific investigations began there with his work on Texas Fever with Dr. John Waldo Connaway in 1900,

and as a fellow in Physiology and Pharmacology under Dr. Charles Wilson Greene in 1901. In 1902 he went to Western Reserve University in the laboratory of Dr. George Neil Stewart as a Demonstrator in Physiology, and then to the University of Chicago as Instructor in 1903.

In 1904 he married Maude Glidden Walker of Indianapolis (now deceased). Their only child, a son, Charles Claude Guthrie, Jr., is now Sales Promotion Manager of the *New York Times*.

Alexis Carrel came to the University of Chicago in 1905 and the two began their joint work on blood vessel anastomosis and organ transplantation. As noted, their association ended after about 15 months when Dr. Guthrie was appointed Head of the Departments of Physiology and Pharmacology at the School of Medicine of Washington University, St. Louis, but the two men corresponded very frequently for the next several years. In 1907 Guthrie was awarded the degree of Doctor of Philosophy from Chicago. In 1909 he accepted the Chair of Physiology and Pharmacology at the University of Pittsburgh, a position he was to hold for over 40 years. Pittsburgh awarded him an honorary Sc.D. in 1935.

In 1907 he was joined by his sister Fannie, who had received the A.B., B.S. and A.M. degrees from the University of Missouri. Until 1913 she participated in all phases of his surgical and other experimental work, and helped him draft the manuscript for the book on blood vessel surgery. During World War I he remained at the University as an essential teacher, but served under the Surgeon General on the Committee on Shock, remaining in the Medical Reserve as a Major until 1940. During his professorship at the University of Pittsburgh he was an inspiration to many students. One of these, Dr. Harold A. Kipp currently on the surgical faculty, has kindly supplied the following personal account of his association.

"Doctor Guthrie established two teaching fellowships in the department of Physiology at the Medical School. These were available to those in whom he suspected the existence of a grain of talent and interest in Physiology and began in the third year. The opportunities brought students into close relation with a man of complete integrity, basic simplicity and unique originality. The selected fellows became completely devoted to him.

"Guthrie has been considered by some of his surviving contemporaries as a graduate student's physiologist. He was eminently able to direct the development of ideas his students might present and to prevent wasting their time on previously achieved results. It is regrettable that

the present opportunities for subsidization of basic research were not available in his active years. On several occasions, over a period of years, plans for the establishment of a laboratory of clinical and particularly surgical research were drawn, but no support was available for their development. It is interesting to speculate upon the development of clinical vascular operations had he had adequate support.

"Since he possessed a remarkable mechanical ability many of the instruments used by the students in the physiology laboratory were designed and made in his own workshop. The course in physiology was planned to teach fundamentals, with an introduction to their clinical application. Students were stimulated to pursue further basic investigation either as a contribution to clinical knowledge or towards a career in Physiology.

"Doctor Guthrie's gentleness was exemplified in all his teaching. Any rough or careless treatment of animals or their tissues brought upon the student a storm of reproof that could not fail to impress. This characteristic, of course, explains in large measure his outstanding technical success in the meticulous field of vascular surgery.

"I shall always remember him as an inspiring teacher and investigator. My gratitude for his friendship and appreciation of his guidance have continued to the present."

Dr. Guthrie's scientific interests were always wide-ranging, as can readily be seen from his bibliography. He wrote on subjects all the way from "Physiologic Lensless Spectacles," shock and resuscitation, the anesthetic properties of magnesium salts, and graft hybrids, to "What Mathematical Subjects should be included in the Curriculum of the College," and even on "Science and Religion."

He still has much experimental material, including manuscripts—complete even to graphs and tables, never submitted for publication. Among the most comprehensive of these are:

1. Fundamental studies of the physiology of skeletal muscle, nerves, smooth muscle and heart, with special studies of the latter showing their importance in interpretation of heart irregularities and other disorders.

2. Very extensive and comprehensive studies of the quantitative composition of bloods, particularly of ox, dog, rabbit, and man, by simple, rapid and accurate physical methods, requiring very small quantities of blood, and therefore, suitable for clinical use.

The accumulation of this unpublished material was due to the time-consuming nature of the experimental work involved—including extensive comparative studies of current methods, and planning and testing

new methods and apparatus after constructing it. There were extensive interruptions from special school assignments other than departmental, e.g. hospital planning (practically two years); three periods of extensive building reconstruction and one complete departmental transfer to another building, amounting to three or four more years; four years of war; and, finally, impaired health.

In 1950 he became Professor Emeritus and a short time afterwards returned to Columbia, Missouri where he now lives with his sister. The family still owns the original farm and "homestead" in St. Charles County.

BIBLIOGRAPHY

C. C. Guthrie, M.D.

1. The Laking of Dried Red Blood-Corpuscles.
   By C. C. GUTHRIE.
   American Jour. of Physiology, 1903, VIII, 441.
2. The Influence of Formaldehyde on the Action of Certain Laking Agents and on Coagulation of Blood.
   By C. C. GUTHRIE.
   American Jour. of Physiology, 1903, IX, 187.
3. An Improved Mercury Manometer.
   By C. C. GUTHRIE.
   Jour. of the American Medical Association, November 14, 1903, XLI, 1209.
4. A Serviceable Form of Capillary Electrometer.
   By C. C. GUTHRIE.
   Jour. of the American Medical Association, January 16, 1904, XLII, 173.
5. The Effect of the Intravenous Injection of Formaldehyde and Calcium Chloride on the Haemolytic Power of Serum.
   By C. C. GUTHRIE.
   Americal Jour. of Physiology, 1904, XII, 139.
6. A Contribution to the Clinical Knowledge of Texas Fever.
   By C. C. GUTHRIE.
   Jour. of Infectious Diseases, 1905, II, 529-554.
7. The Effects of Intravenous Injections of Bone Marrow Extracts upon Blood Pressure.
   By O. H. BROWN and C. C. GUTHRIE.
   American Jour. of Physiology, 1905, XIV, 328.
8. Functions of a Transplanted Kidney.
   By ALEXIS CARREL and C. C. GUTHRIE.
   Science, 1905, XXII, 473.
9. Extirpation and Replantation of the Thyroid Gland with Reversal of the Circulation.
   By ALEXIS CARREL and C. C. GUTHRIE.
   Science, 1905, XXII, 535.

10. The Transplantation of Veins and Organs.
By ALEXIS CARREL and C. C. GUTHRIE.
American Medicine, Dec. 1905, X, 1101.

*11. Transplantation Biterminale Complete d'un Segment de Veine sur une Artere.
By ALEXIS CARREL and C. C. GUTHRIE.
Comptes Rendus de Biologie, 1905, LIX, 412.

*12. Extirpation et Replantation de la Glande Thyroide avec Reversion de la Circulation.
By ALEXIS CARREL and C. C. GUTHRIE.
Comptes Rendus de Biologie, 1905, LIX, 413.

13. Experiments on Resuscitation.
By C. C. GUTHRIE and G. N. STEWART.
Science, N.S. XXI, 1905.

14. Anastomosis and Transplantation of Blood Vessels.
By C. C. GUTHRIE and ALEXIS CARREL.
Amer. Med., X, 284, Aug., 1905.

15. The Reversal of the Circulation in a Limb.
By C. C. GUTHRIE and ALEXIS CARREL.
Annals of Surgery, XLIII, 203, 1906.

16. Augmentation Artificiale de la Circulation dans les Glandes Pathologiques.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. de Soc. de Biol. LX, 582, 1906.

17. Anatomical Results of Biterminal Venous Transplantations.
By C. C. GUTHRIE and ALEXIS CARREL.
Am. Jr. Med. Sciences, Vol. 132, 4.5, Sept., 1906.

18. Arterio-sclerose per Modification Chirurgicale de la Circulation.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. Soc de Biol. LX, 730, 1906.

19. Resultats Eloignes de la Transplantationen Veineuse Uniterminale.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. Soc. de Biol., LX, 529, 1906.

20. A New Method of Anastomosis of Blood Vessels and Its Application to the Replantation and Transplantation of the Blood Vessels, Limbs and Organs.
By C. C. GUTHRIE and ALEXIS CARREL.
XVth Congress International de Med., Lisbon, 1906.

*out of print

21. L'excision Longitudinale des Vaisseaux et ses Resultates.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. Soc. de Biol., LX, 984, 1906.

22. Resultates du Patching des Arteries.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. Soc. de Biol., LX, 1009, 1906.

23. Transplantations des deus reins d'un chien une chienne les deux reins sont extirpes.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. Soc. de Biol., LX, 465, 1906.

24. Technique de la transplantation homoplastique de l'ovarie.
By C. C. GUTHRIE and ALEXIS CARREL.
Compt. Rend. Soc. de Biol., LX, 465, 1906.

25. The Nutrition of the Excised Mammalian Heart. Eine vorlaufige Metteilung.
By C. C. GUTHRIE and F. H. PIKE.
Biophys. Centralbl., II, 151, 1906.

26. Complete Amputation of the Thigh, with Replantation.
By ALEXIS CARREL and C. C. GUTHRIE.
American Journal of the Medical Sciences, February, 1906, Vol. 131, p. 297.

27. Uniterminal and Biterminal Venous Transplantations.
By ALEXIS CARREL and C. C. GUTHRIE.
Surgery, Gynecology and Obstetrics, 1906, II, 266.

28. Results of a Replantation of the Thigh.
By ALEXIS CARREL and C. C. GUTHRIE.
Science, 1906, XXIII, 393.

29. Successful Transplantation of Both Kidneys from a Dog into a Bitch with Removal of Both Normal Kidneys from the Latter.
By ALEXIS CARREL and C. C. GUTHRIE.
Science, 1906, XXIII, 394.

30. The Resuscitation of the Central Nervous System of Mammals.
By G. N. STEWART, C. C. GUTHRIE, R. L. BURNS, and F. H. PIKE.
Jour. of Experimental Medicine, 1906, VIII, 289.

31. A New Method for the Homoplastic Transplantation of the Ovary.
By ALEXIS CARREL and C. C. GUTHRIE.
Science, 1906, XXIII, 591.

32. The Relation of Pressure in the Coronary Vessels to the Activity of the Isolated Heart, and Some Closely Related Problems.
By C. C. GUTHRIE and F. H. PIKE.
Science, 1906, XXIV, 52.

33. The Effect of Changes in Blood Pressure on Respiratory Movements.
By C. C. GUTHRIE and F. H. PIKE.
American Journal of Physiology, 1906, XVI, 475.

34. The Maintenance of Cerebral Activity in Mammals by Artificial Circulation.
By C. C. GUTHRIE, F. H. PIKE and G. N. STEWART.
American Journal of Physiology, 1906, XVII, 344.

35. The Relation of the Activity of the Excised Mammalian Heart to Pressure in the Coronary Vessels and to Its Nutrition.
By C. C. GUTHRIE and F. H. PIKE.
American Journal of Physiology, 1907, XVIII, 14.

36. Respiratory Valves.
By C. C. GUTHRIE.
Jour. of American Medical Assn., 1907, XLVIII, 1183.

37. Surgical Rooms of the Department of Physiology and Pharmacology.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, June, 1907.

38. A Study of the Relative Efficiency of Various Solutions on the Activity of the Isolated Mammalian Heart.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, June, 1907, V. 155.

39. Results of Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, 1907, VI, 45.

40. Heterotransplantations of Blood Vessels.
By C. C. GUTHRIE.
American Jour. of Physiology, 1907, XIX, 482.

41. Results of Removal and Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Proc. Amer. Phys. Soc., *Amer. Jour. Phys.* XVI, 19, 1907.

42. Transplantations d'ovaries practique avec success chez le poule.
By C. C. GUTHRIE.
Arch. Internal de Phys., V, 108, 1907.

43. Results of Heterotransplantations of Blood Vessels.
By C. C. GUTHRIE.
Quarterly Bul. Med. Dept. Washington Univ., VI, 39, 1907.

44. Survival of Tissues and Organs under Perfusion.
By C. C. GUTHRIE.
Proc. of Amer. Phys. Soc., *Amer. Journal of Phys.*, XXI, p. xvi, 1908.

45. Further Results of Heterotransplantations of Blood Vessels.
Proc. Amer. Phys. Soc., *Amer. Jour. Phys.*, XXI, p. xvii, 1908.

46. Further Observations on the Relation Between Blood Pressure and Respiratory Movements.
By C. C. GUTHRIE and F. H. PIKE.
American Journal of Physiology, 1908, XX, 451.

47. Further Results of Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Journal of Experimental Zoology, 1908, V. 563.

48. Studies in Resuscitation: I. The General Conditions Affecting Resuscitation, and the Resuscitation of the Blood and of the Heart.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
Journal of Experimental Medicine, 1908, X, 371.

49. Studies in Resuscitation: II. The Reflex Excitability of the Brain and Spinal Cord After Cerebral Anemia.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
American Journal of Physiology, 1908, XXI, 359.

50. Studies in Resuscitation: III. The Resuscitation of the Glands and Muscles After Temporary Anaemia.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
American Journal of Physiology, 1908, XXII, 51.

51. Studies in Resuscitation: IV. The Return of Function in the Central Nervous System After Temporary Cerebral Anaemia.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
Journal of Experimental Medicine, 1908, X, 490.

52. Control of Spasms by Asphyxiation.
By A. H. RYAN and C. C. GUTHRIE.
American Journal of Physiology, 1908, XXII, 440.

32. The Relation of Pressure in the Coronary Vessels to the Activity of the Isolated Heart, and Some Closely Related Problems.
By C. C. GUTHRIE and F. H. PIKE.
Science, 1906, XXIV, 52.

33. The Effect of Changes in Blood Pressure on Respiratory Movements.
By C. C. GUTHRIE and F. H. PIKE.
American Journal of Physiology, 1906, XVI, 475.

34. The Maintenance of Cerebral Activity in Mammals by Artificial Circulation.
By C. C. GUTHRIE, F. H. PIKE and G. N. STEWART.
American Journal of Physiology, 1906, XVII, 344.

35. The Relation of the Activity of the Excised Mammalian Heart to Pressure in the Coronary Vessels and to Its Nutrition.
By C. C. GUTHRIE and F. H. PIKE.
American Journal of Physiology, 1907, XVIII, 14.

36. Respiratory Valves.
By C. C. GUTHRIE.
Jour. of American Medical Assn., 1907, XLVIII, 1183.

37. Surgical Rooms of the Department of Physiology and Pharmacology.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, June, 1907.

38. A Study of the Relative Efficiency of Various Solutions on the Activity of the Isolated Mammalian Heart.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, June, 1907, V. 155.

39. Results of Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, 1907, VI, 45.

40. Heterotransplantations of Blood Vessels.
By C. C. GUTHRIE.
American Jour. of Physiology, 1907, XIX, 482.

41. Results of Removal and Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Proc. Amer. Phys. Soc., *Amer. Jour. Phys.* XVI, 19, 1907.

42. Transplantations d'ovaries practique avec success chez le poule.
By C. C. GUTHRIE.
Arch. Internal de Phys., V, 108, 1907.

43. Results of Heterotransplantations of Blood Vessels.
By C. C. GUTHRIE.
Quarterly Bul. Med. Dept. Washington Univ., VI, 39, 1907.

44. Survival of Tissues and Organs under Perfusion.
By C. C. GUTHRIE.
Proc. of Amer. Phys. Soc., *Amer. Journal of Phys.*, XXI, p. xvi, 1908.

45. Further Results of Heterotransplantations of Blood Vessels.
Proc. Amer. Phys. Soc., *Amer. Jour. Phys.*, XXI, p. xvii, 1908.

46. Further Observations on the Relation Between Blood Pressure and Respiratory Movements.
By C. C. GUTHRIE and F. H. PIKE.
American Journal of Physiology, 1908, XX, 451.

47. Further Results of Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Journal of Experimental Zoology, 1908, V. 563.

48. Studies in Resuscitation: I. The General Conditions Affecting Resuscitation, and the Resuscitation of the Blood and of the Heart.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
Journal of Experimental Medicine, 1908, X, 371.

49. Studies in Resuscitation: II. The Reflex Excitability of the Brain and Spinal Cord After Cerebral Anemia.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
American Journal of Physiology, 1908, XXI, 359.

50. Studies in Resuscitation: III. The Resuscitation of the Glands and Muscles After Temporary Anaemia.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
American Journal of Physiology, 1908, XXII, 51.

51. Studies in Resuscitation: IV. The Return of Function in the Central Nervous System After Temporary Cerebral Anaemia.
By F. H. PIKE, C. C. GUTHRIE, and G. N. STEWART.
Journal of Experimental Medicine, 1908, X, 490.

52. Control of Spasms by Asphyxiation.
By A. H. RYAN and C. C. GUTHRIE.
American Journal of Physiology, 1908, XXII, 440.

53. Some Practical Aspects of the Physiology of the Circulation.
By C. C. GUTHRIE.
Interstate Medical Journal, 1908, XV, No. 6.

54. Structural Changes and Survival of Cells, in Transplanted Blood Vessels.
By C. C. GUTHRIE.
Jour. of the American Medical Assn., 1908, L, 1035.

55. Transplantation of Formaldehyde-fixed Blood Vessels.
By C. C. GUTHRIE.
Science, 1908, XXVII, 473.

56. Results of Ovarian Transplantation of Body Weight and Egg Weights in Fowls.
By C. C. GUTHRIE.
Jour. of the American Medical Assn., 1908, LI, 1314.

*57. Some Physiological Aspects of Blood-Vessels Surgery.
By C. C. GUTHRIE.
Jour. of the American Medical Assn., 1908, LI, 1658.

58. The Harmful Action of "Physiological" Salt Solutions on Animal Tissues.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, 1908, VII, 40.

59. Fate of Transplanted Blood Vessels.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, 1908, VII, 49.

60. Further Results of Transplantation of Ovaries in Chickens.
By C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, 1908, VII, 51.

61. On the Relation of Circulation of Spasms.
By A. H. RYAN and C. C. GUTHRIE.
Quarterly Bulletin of the Medical Department of Washington University, 1908, VII, 58.

62. On Misleading Statements.
By C. C. GUTHRIE.
Science, 1909, XXIX, 29.

*out of print

63. Guinea Pig Graft-Hybrids.
By C. C. GUTHRIE.
Science, 1909, XXX, 724.

64. Suture of Blood-Vessels with Human Hair.
By F. V. GUTHRIE and C. C. GUTHRIE.
Jour. of the American Medical Assn., 1910, LIV, 349.

65. The Effect on the Kidneys of Temporary Anaemia, Alone and Accompanied by Perfusion.
By C. C. GUTHRIE.
Archives of Internal Medicine, 1910, V, 232.

66. The Effect of Asphyxia on the Pupil.
By C. C. GUTHRIE, F. V. GUTHRIE, and A. H. RYAN.
Science, 1910, XXXI, 395.

67. Survival of Engrafted Tissues. I. (A) Ovaries and (B) Testicles.
By C. C. GUTHRIE.
Journal of Experimental Medicine, 1910, XII, 269.

68. Survival of Engrafted Tissues. II. (A) Thyroid (Including Parathyroid); (B) Kidney (Including Adrenal).
By C. C. GUTHRIE.
Jour. of the American Medical Assn., 1910, LIV, 831.

69. Survival of Engrafted Tissues. III. Blood-Vessels.
By C. C. GUTHRIE.
Heart, 1910, II, 115.

70. The Action of Magnesium Salts: A. In Relation to Motor Nerve Impulses; B. In Relation to Sensory Stimulation.
By A. H. RYAN, F. V. GUTHRIE, and C. C. GUTHRIE.
Proc. of Soc. for Exper. Biol. & Med., 1910, VII, 39.

71. The Effects of Direct Application of Magnesium Salts: A. To Motor Sensory Nerves; B. To Cardio-inhibitory Nerves.
By C. C. GUTHRIE, F. V. GUTHRIE, and A. H. RYAN.
Proc. of Soc. for Exp. Biol. & Med., 1910, VII, 41.

72. The Survival and Growth of Subcutaneously Engrafted Ovarian and Testicular Tissue.
By C. C. GUTHRIE.
Proc. of Soc. for Exp. Biol. & Med., 1910, VII, 43.

73. The Survival of Engrafted Thyroid and Renal Tissue.
By C. C. GUTHRIE.
Proc. Soc. for Exp. Biol. & Med., 1910, VII, 44.

74. Effect of Anaemia and of Double Hyperemia on Hyperplastic Goiter.
By C. C. Guthrie.
Proc. Soc. for Exp. Biol. & Med., 1910, VII, 45.

75. On the Alleged Specific Anaesthetic Properties of Magnesium Salts.
By C. C. Guthrie and A. H. Ryan.
American Jour. of Physiology, 1910, XXVI, 329.

76. On the Insufflation of the Lungs with Hydrogen; with Carbon Dioxide; and with Air.
By C. C. Guthrie, F. V. Guthrie, and A. H. Ryan.
Jour. of Pharmacology & Experimental Therapeutics, 1910, II, 49.

77. Further Observations on the Structure of Anastomosed Blood Vessels.
By C. C. Guthrie.
Proc. Soc. for Exp. Biol. & Med., 1910, VII, 151.

78. Intravenous Foreign Bodies.
By C. C. Guthrie and A. H. Ryan.
Proc. Soc. for Exp. Biol. & Med., 1911, IX, 31.

79. Uber Ausschaltung der hoheren Zentren zu physiologischen Zwecken.
By C. C. Guthrie.
Zeitsch. f. Biol. Technik u. Methodik, 1911, II, 138.

80. On Graft Hybrids.
By C. C. Guthrie.
Annual Report American Breeders Association, 1911, VI, 356.

81. Transplantation of Germinal Elements in Poultry.
By C. C. Guthrie.
Proc. Internat. Assn. of Instructors & Investigators in Poultry Husbandry, Ithaca, N. Y., Aug. 1911.

82. Alterations of the Circulation on Goitre.
By C. C. Guthrie and A. H. Ryan.
Interstate Medical Journal, 1911, XVIII.

83. On Evidence of Soma Influence on Offspring from Engrafted from Ovarian Tissue.
By C. C. Guthrie.
Science, 1911, XXXIII, 816.

84. Respiration Valves.
By C. C. GUTHRIE.
Jour. of American Medical Assn., 1911, LVII, 887.

85. Transplantation of Ovaries.
By C. C. GUTHRIE.
Science, 1911, XXXIV, 918.

*86. Vascular Suture and Some Considerations Regarding Its Successful Execution and Application.
By C. C. GUTHRIE.
Cleveland Medical Journal, 1912, XI, 317.

87. Physiology of the Heart.
By C. C. GUTHRIE.
Pennsylvania Medical Journal, November, 1912.

88. *Monograph: Blood-Vessel Surgery and Its Applications.*
By C. C. GUTHRIE.
Edward Arnold, London, 1912, 360 pages.

89. What Mathematical Subjects Should Be Included in the Curriculum of the College?
By C. C. GUTHRIE.
The Mathematics Teacher, 1913, VI, 100.

90. Weight Fluctuations in Frogs.
By C. C. GUTHRIE and F. V. GUTHRIE (by invitation).
Proc. Soc. for Exp. Biol. & Med., 1914, XI, 144.

91. The Sensory Effect of Local Application of Hypertonic Salt Solutions.
By C. C. GUTHRIE and M. E. LEE (by invitation).
Proc. Soc. for Exp. Biol. & Med., 1914, XI, 146.

92. The Blood in "Shock."
By C. C. GUTHRIE and F. V. GUTHRIE (by invitation).
Proc. Soc. for Exp. Biol. & Med. 1914, XI, 148.

93. Laking of Blood by Hypertonic Solutions.
By C. C. GUTHRIE and M. E. LEE (by invitation).
Proc. Soc. for Exp. Biol. & Med., 1914, XI, 149.

94. Laking of Blood by Freezing and Thawing.
By C. C. GUTHRIE and M. E. LEE (by invitation).
Proc. Soc. for Exp. Biol. & Med., 1914, XI, 150.

*out of print

. Laking of Blood By Drying.
By C. C. GUTHRIE and M. E. LEE (by invitation).
Proc. Soc. for Exp. Biol. & Med., 1914, XI, 151.

96. Ovarian Transplantation.
By C. C. GUTHRIE and M. E. LEE.
Jour. of American Medical Assn., 1915, LXIV, 1823.

97. Contributions to Practical Physiology and Pharmacology.
By C. C. GUTHRIE.
Published and Presented by the Writer, 1915.

98. Muscular Irritability.
By C. C. GUTHRIE.
American Jour. of Physiology, XLII, 598, 1917.

99. Digitalis on Cardiac Irritability.
By C. C. GUTHRIE.
Jour. of Pharmacology & Experimental Therapeutics, 1917, IX, 342.

100. Experimental Shock.
By C. C. GUTHRIE.
Jour. of American Medical Association, 1917. LXIX, 1394.

101. A Tentative Explanation of the Mechanism of Hemolysis Associated with Loss of Water, and the Bearing of the Phenomenon on Certain Biology Problems.
By C. C. GUTHRIE.
Jour. of Laboratory & Clinical Medicine, 1917, III, 87.

102. The Interpretation of the Manifestations of Shock.
By C. C. GUTHRIE.
Pennsylvania Medical Journal, 1918, XXII, 123.

103. Observations in Shock.
By C. C. GUTHRIE.
American Jour. of Physiology, 1918, XLV, 544.

104. The Blood in Shock.
By C. C. GUTHRIE.
Archives of Internal Medicine, 1918, XXII, 1.

105. End-Results of Arterial Restitution with Devitalized Tissue.
By C. C. GUTHRIE.
Jour. of American Medical Assn., 1919, LXXIII, 186.

106. The Blood in Clinical Shock.
By C. C. GUTHRIE and G. C. WEIL.
American Journal of Physiology, 1920, LI, 194.

107. Report on The Teaching of Physiology.
By C. C. GUTHRIE.
Assoc. Am. Med. Colleges, March, 1920, p. 69.

108. A Method for Determining the Rate of Oxygen Absorption by Blood.
By C. C. GUTHRIE and W. S. MCELLROY.
American Journal of Physiology, 1920, LI, 195.

109. Physiological and Physiological Chemical Observations in Epidemic Influenza.
By C. C. GUTHRIE.
Monograph on Epidemic Influenza. University of Pittsburgh, 1920.

110. A Simplified Form of Apparatus for Air Analysis.
By C. C. GUTHRIE.
Jour. of Biological Chemistry, 1921, XLVIII, 365.

111. A Simple and Accurate Metabolism Spirometer. Spirometer Measurements of Oxygen Consumption by the Rebreathing Method.
By C. C. GUTHRIE.
Archives of Internal Medicine, 1921, XXVIII, 841.

112. A Gas Receiver of Convenient and Practical Form for Sampling Expired Air for Analysis.
By C. C. GUTHRIE.
Jour. of Biological Chemistry, 1921, XLVIII, 373.

113. A Spirometer for Continuously and Accurately Measuring Expired Air and Sampling for Analysis.
By C. C. GUTHRIE.
Jour. of Laboratory & Clinical Medicine, 1922, VII, 421.

114. Results on an Enlarged Thyroid Gland Nine Years After Obstructing the Veins.
By C. C. GUTHRIE.
American Journal of Physiology, 1922, LIX, 447.

115. End Results of Arterial Transplants.
By C. C. GUTHRIE, O. KLOTZ, and H. H. PERMAR.
Annals of Surgery, 1923, LXXVIII, 305.

116. Twenty-Five Years Progress in Physiology and Pharmacology.
By C. C. GUTHRIE.
Proc. Congress of Med. Ed., Licensure, Pub. Health & Hospitals, Chicago, March 9-12, 1925.

117. Respiration in Fowls.
By C. C. GUTHRIE.
American Jour. of Physiology, 1926, LXXVI, 204.

118. Blood Gas Analyzer.
By C. C. GUTHRIE.
Jour. of Lab. & Clinical Medicine, 1926, XI, #6.

119. Studies on the Rate of Oxygen Absorption by Blood.
By C. C. GUTHRIE and W. S. MCELLROY.
Jour. of Biological Chemistry, 1927, LXXIV, 25.

120. Methemoglobinemia.
By C. C. GUTHRIE, T. K. KRUSE, and W. S. MCELLROY.
Jour. of Pharmacology & Experimental Therapeutics, 19
XXXI, 208.

121. Refractory Period of Heart.
By C. C. GUTHRIE.
American Journal of Physiology, 1927, LXXXI, 483.

122. An Apparatus for Quickly Measuring the Specific Gr
Body Fluids.
By C. C. GUTHRIE.
Jour. of Lab. & Clinical Medicine, 1932, XVII, 1158.

123. A Split Second Timer.
By C. C. GUTHRIE.
Jour. of Lab. & Clinical Medicine, 1932, XVII, 376.

124. Protective Amputation of Limbs by Stagomantis Car
By C. C. GUTHRIE.
Science, 1933, LXXVIII, 146.

125. Swarming and Mating of Ants.
By C. C. GUTHRIE.
Science, LXXVII, 627, 1933.

126. Functional Heart Mechanisms.
By C. C. GUTHRIE.
Proc. Soc. for Experimental Biol. & Med., 1933, XX

127. Physiologic Lensless Spectacles.
By C. C. GUTHRIE.
Archives of Opthalmology, 1931, XI, 251.

128. *Brochure.* Science and Religion.
By C. C. GUTHRIE.
Published by the Writer, 1934.

129. Cause and Prevention of a Type of Leg Deformity in Brooder-Raised Chicks.
By C. C. Guthrie.
Federation Proceedings, 1946, V, 39.

130. The Quantitative Effect of Hemorrhage on Plasma Proteins.
By C. C. Guthrie and Marian E. Lee.
Federation Proceedings, 1948, VII, 46.

131. *Laboratory Directions in Experimental Physiology.*
By C. C. Guthrie.
Edwards Bros., Ann Arbor, Michigan, 1941; 2nd Ed. 1947; 3rd Ed. 1958.

117. Respiration in Fowls.
By C. C. GUTHRIE.
American Jour. of Physiology, 1926, LXXVI, 204.

118. Blood Gas Analyzer.
By C. C. GUTHRIE.
Jour. of Lab. & Clinical Medicine, 1926, XI, #6.

119. Studies on the Rate of Oxygen Absorption by Blood.
By C. C. GUTHRIE and W. S. McELLROY.
Jour. of Biological Chemistry, 1927, LXXIV, 25.

120. Methemoglobinemia.
By C. C. GUTHRIE, T. K. KRUSE, and W. S. McELLROY.
Jour. of Pharmacology & Experimental Therapeutics, 1927, XXXI, 208.

121. Refractory Period of Heart.
By C. C. GUTHRIE.
American Journal of Physiology, 1927, LXXXI, 483.

122. An Apparatus for Quickly Measuring the Specific Gravity of Body Fluids.
By C. C. GUTHRIE.
Jour. of Lab. & Clinical Medicine, 1932, XVII, 1158.

123. A Split Second Timer.
By C. C. GUTHRIE.
Jour. of Lab. & Clinical Medicine, 1932, XVII, 376.

124. Protective Amputation of Limbs by Stagomantis Carolina.
By C. C. GUTHRIE.
Science, 1933, LXXVIII, 146.

125. Swarming and Mating of Ants.
By C. C. GUTHRIE.
Science, LXXVII, 627, 1933.

126. Functional Heart Mechanisms.
By C. C. GUTHRIE.
Proc. Soc. for Experimental Biol. & Med., 1933, XXX, 946.

127. Physiologic Lensless Spectacles.
By C. C. GUTHRIE.
Archives of Opthalmology, 1934, XI, 254.

128. *Brochure.* Science and Religion.
By C. C. GUTHRIE.
Published by the Writer, 1934.

129. Cause and Prevention of a Type of Leg Deformity in Brooder-Raised Chicks.
By C. C. GUTHRIE.
Federation Proceedings, 1916, V, 39.

130. The Quantitative Effect of Hemorrhage on Plasma Proteins.
By C. C. GUTHRIE and MARIAN E. LEE.
Federation Proceedings, 1918, VII, 46.

131. *Laboratory Directions in Experimental Physiology.*
By C. C. GUTHRIE.
Edwards Bros., Ann Arbor, Michigan, 1941; 2nd Ed. 1947; 3rd Ed. 1958.